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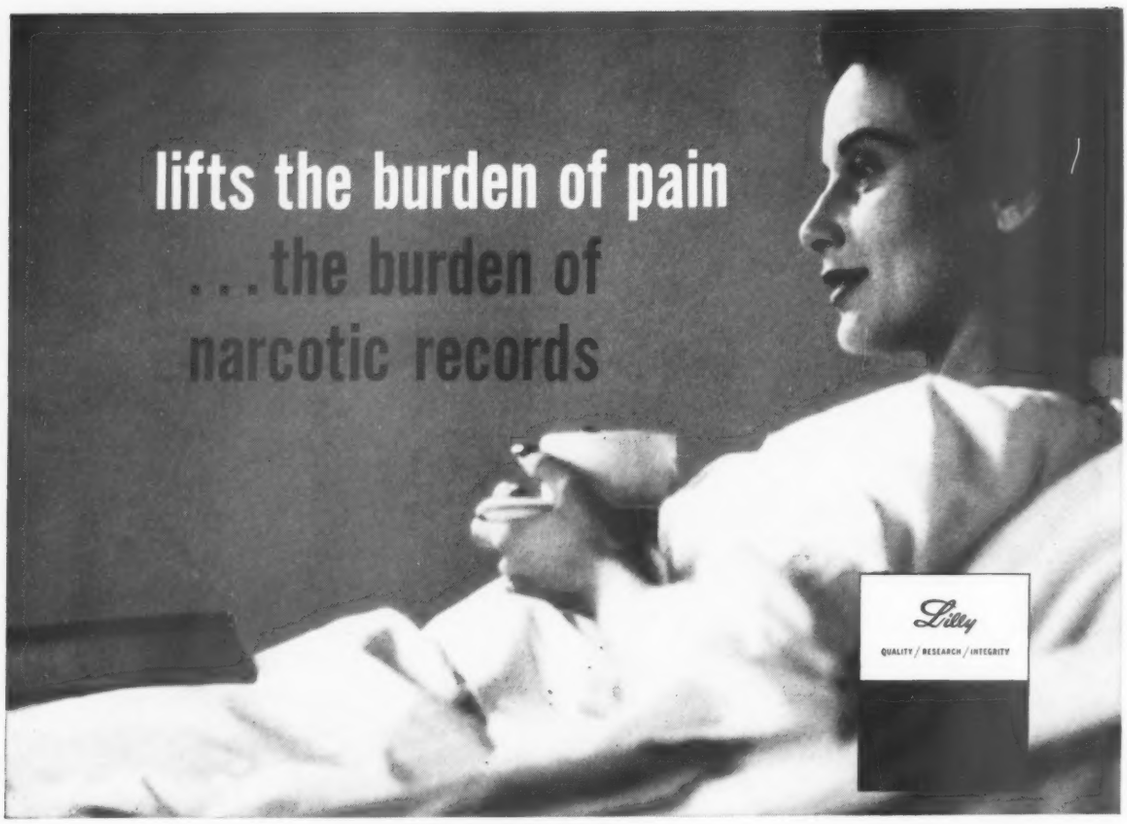
American Journal of Hospital Pharmacy

Official publication of the American Society of Hospital Pharmacists

FORMERLY The BULLETIN

JUST A LITTLE PIECE OF PAPER



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Dear Sirs:

Interest in Evaluation of Service

DEAR SIRS: The article "Evaluation of a Pharmaceutical Service in Hospitals" which appears in the August issue of the JOURNAL has much value as a tool for self evaluation. Although the outline is specifically designed for United States Public Health Service installations, we feel that it can and should be utilized by pharmacists in the voluntary hospital system.

This article is so rich in thought stimulating material which can improve hospital pharmacy services, that Dr. Rourke would like to obtain six reprints, if available, for distribution to all of our staff members. Please enclose your statement for any charges involved.

THOMAS P. FAILEY, *Hospital Consultant*

Anthony J. J. Rourke, M.D.
Hospital Consultant
26 Overlook Circle
New Rochelle, New York

DEAR SIRS: I would like to receive two copies of the article "Evaluation of a Pharmaceutical Service in Hospitals" by Dr. George F. Archambault . . .

Thank you for your service, I remain,

GERARD L. PIERCE, *Captain, MSC*

Chief, Pharmacy Service
Madigan Army Hospital
Tacoma, Washington

DEAR SIRS: I would like to have a copy of the article entitled "Evaluation of a Pharmaceutical Service in Hospitals" . . .

GEORGE A. TOTH, *Pharmacist*

Conemaugh Valley Memorial Hospital
Johnstown, Pennsylvania

Barbiturate and Narcotic Control

DEAR SIRS: We are studying our method of control of barbiturates and narcotics on the nursing floors, as well as in the pharmacy. Would you please advise me whether or not the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS has any recommended procedures and forms for the control and charging of narcotics and barbiturates.

JOHN W. COLBY, *Administrator*

St. Luke's Hospital
Spokane 11, Washington

EDITOR'S NOTE: The AMERICAN SOCIETY OF HOSPITAL PHARMACISTS has available a reprint entitled "Suggested Regulations for Handling Narcotics in Hospital," which outlines accepted procedures for handling narcotics. From the standpoint of records, similar procedures have been applied to the control of barbiturates in some hospitals.

Copies of the reprint are available from the Division of Hospital Pharmacy of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and the American Pharmaceutical Association, 2215 Constitution Ave., N.W., Washington 7, D. C.

Author Comments

DEAR SIRS: I received the tear sheets of my article entitled "Physician-Pharmacist Team Plays Key Roles in Drug Evaluation" which appeared in the May (1959) issue of your publication. I appreciate the excellent way in which the article was made up.

ABRAHAM GELPERIN, M.D.

Director of Health and Hospitals
City of Kansas City, Missouri
Kansas City, Missouri

Interest in Formulary Service

DEAR SIRS: Please send to the above address fifteen copies of the American Hospital Formulary Service. This is an excellent publication and our Pharmacy and Therapeutics Committee has unanimously accepted it as our official formulary.

Thanks very much for all your efforts and may you have continued success in making hospital pharmacy a leader in our profession.

VINCENT J. CONTI, *Chief Pharmacist*

New York Society for the Relief of the Ruptured and Crippled
The Hospital for Special Surgery
Margaret M. Caspary Clinic
New York, New York

DEAR SIRS: I would appreciate your send a copy of the article entitled "Suggestions on the Use of the American Hospital Formulary Service" . . .

WILLIAM D. GIBSON, *Administrator*

Decatur County Memorial Hospital
Greensburg, Indiana

DEAR SIRS: I am interested in obtaining a copy of the AMERICAN HOSPITAL FORMULARY SERVICE. What is the cost of the publication.

E. T. SCHNOOR, M.D.

3718 Delverne Road
Baltimore, Maryland

EDITOR'S NOTE: The American Hospital Formulary Service may be ordered from The Hamilton Press, Hamilton, Illinois, at $15.00 per copy.

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by DON E. FRANCKE

International Pharmacopoeia-- A World-Wide Service

► PUBLICATION OF THE FIRST SUPPLEMENT to the *International Pharmacopoeia* calls attention to the splendid work being done by the World Health Organization in supplying recommended specifications for pharmaceuticals. The usefulness of this service to the community of nations can be readily appreciated when one considers that drugs are the most widely used therapeutic tools for the diagnosis, prevention and treatment of disease and that more than one-half of the 90 member nations of WHO have not developed a national pharmacopeia of their own. Although the standards suggested by the *International Pharmacopoeia* do not, as such, have legal status, they are freely available to all countries for adoption and use, with or without modification, as authorities in the individual countries decide.

The First Supplement to Volumes I and II of the *International Pharmacopoeia* contains suggested monographs for 94 drugs or pharmaceutical preparations. Thus the number of monographs issued to date totals 529, with 218 appearing in Volume I and 217 included in Volume II. In addition, 86 appendices have been compiled and published with the volumes.

Several of the appendices of the First Supplement are of special interest to hospital pharmacists. For example, the Table of Usual and Maximal Doses for Adults will serve as a useful reference since it indicates the route of administration, the usual single dose and usual maximal dose, and the maximal single dose and the maximal daily dose. Certain precautionary statements or observations are also made in the table. In addition, there is a Table of Usual Daily Doses for Children containing information which is often difficult to find readily. Doses are those usually given to children "up to 30 months" and "from 30 months to 15 years." This table also lists the mode of administration and precautionary statements. Another appendix of interest is one related to the preparation of isotonic solutions, with several helpful graphs which greatly simplify calculations. The appendix devoted to International Biological Standards and International Biological Reference Preparations is also a useful reference tool, containing as it does reference standards expressed in units of various antigens, antibodies, antibiotics, hormones, and miscellaneous preparations.

While the task of compiling a national pharmacopeia is great, the work of issuing an international set of suggested standards is indeed formidable. In the latter instance the task is made more difficult by the desire to let the voice of each of the 90 member nations of WHO be heard and by the obvious difficulties of conducting discussions and correspondence in many languages.

The work of compiling the *International Pharmacopoeia* is dealt with by Expert Committees on the International Pharmacopoeia and corresponding Sub-Committees on Non-Proprietary Names, together with advisory panels and study groups. Specifications suggested by these groups are sent to all member countries of WHO for comment. Comments received are discussed by the members of the commissions and, where indicated, suitable amendments to the text are made. Coordinating the work of all of these individuals is the task of Mr. Paul Blanc, the Chief Pharmaceutical Officer of WHO, who functions as Secretary to the various Expert Committees and Study-Groups. His is, indeed, a difficult task but one which he has carried out in an admirable manner.

Truly a work of international collaboration, the First Supplement to the *International Pharmacopoeia* represents the efforts of 33 representatives from 17 nations, together with numerous additional advisors from many lands. United States representatives who served as members of Expert Committees in preparing the First Supplement include Mr. G. P. Larrick, Dr. F. A. Maurina, Dr. L. C. Miller, Dr. J. L. Powers, and Dr. R. T. Stormont. Drs. Powers and Miller were also active participants in the preparation of Volumes I and II of the *International Pharmacopoeia* and, of course, one must recognize the great contributions of Dr. E. F. Cook, now retired, who helped make the *International Pharmacopoeia* a reality.

The fact that two volumes and a supplement of the *International Pharmacopoeia* have been published speaks eloquently for those whose pooled knowledge has made possible this important work of international collaboration for world health.

Orders for the *International Pharmacopoeia* may be addressed to the World Health Organization, Sales Section, Palais des Nations, Geneva Switzerland or to Columbia University Press, International Documents Service, 2960 Broadway, New York 27, N. Y.

Rx

C D Leake

JUST A LITTLE PIECE OF PAPER

by ALBERT H. HOLLAND, JR.

► THIS IS THE FIRST OPPORTUNITY I have had to address this SOCIETY, and I am grateful for the privilege.

I have long felt that hospital pharmacy occupies a unique status within your profession. Fortunately, it provides many contacts and opportunities for service which are denied to some of your colleagues. The role of the pharmacist on many of the hospital committees seems to me to be recognition of the essential character of your profession; essential to the hospital, essential to the physician, and most important of all, essential to the patient—the sick human being whom we all are dedicated to serve.

Sometimes I have the feeling that most of us, on occasion, become so preoccupied and engrossed in our immediate problems and day to day activities that we forget the fact that the hospital exists solely for the care and support of the patient, and not *vice versa*. While routine is necessary for the conduct of any large group effort, routine must never become so dominant as to impede progress and deter improvements, or to confuse conformity with successful operation and service.

These are principles which I'm certain all of us can and do accept and endorse. But it is well to reflect now and then, to be sure that we practice what we preach. It is more important to provide good patient care than to make the "system" work perfectly.

Perhaps you are wondering about the title of this talk—"Just a Little Piece of Paper." Have you ever stopped to think how many of the momentous events in world history evolve from, or revolve around a "little piece of paper"?—the *Magna Carta*, the *Bill of Rights*, the *Declaration of Independence*, and our great *Constitution of the United States*, just to mention a few. Yet their influence on man's course on earth and human freedom is so vast as to make true evaluation al-

ALBERT H. HOLLAND, JR., M.D. is with American Home Products Corporation, New York, N. Y.

Presented at the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, August 17, 1959, Cincinnati, Ohio.

most impossible. As our civilization has progressed and man's knowledge increased, we have become even more dependent, reliant if you will, on "little pieces of paper."

The tremendous complexities of government, of the business world, of the physical and biological sciences, could not be properly recorded, or in fact conducted, were it not for myriads of "little pieces of paper." To be more specific, all of us devoted to the care of the sick are, in our own ways, concerned with these "little pieces of paper." For example, the written prescription, the orders on a patient's hospital chart, the advertising and educational material promulgated by the drug industry, the hospital formulary; each is "just a little piece of paper," each may have profound effects upon our lives and the lives of others.

Advertising and Educational Material

Let me dwell, if I may, a bit longer on two of these items. The first, advertising and educational material promulgated by the drug industry. Good friends of mine have indicated their occasional displeasure at receiving drug advertising material in the hospital pharmacy. Perhaps this can be better stated by saying that the hospital pharmacist would prefer having more scientific product information at his disposal and fewer advertising pieces. Personally, I feel that you should have both. The alert, progressive hospital pharmacist should want to know what kind of advertising is being sent to the physicians on his medical staff.

It is imperative that you keep up-to-date and fully informed of the latest developments and drug improvements if you are to exercise your professional responsibilities to both physician and patient, and to the hospital administration. In my judgement, this can not be adequately accomplished on a current basis if you reject advertising and wait only for the appearance of formal papers in the medical literature. It is unfortunate, but true, that almost all good medical journals have such a backlog of papers that early publication can rarely be anticipated. Medical advertising, therefore, assumes an extremely important role as a perfectly legitimate means of communication.

While we are on this subject, let's dispense with the all too prevalent belief that advertising is something wrong, bad, deceitful, wasteful, or immoral. Of course in the hands of the unscrupulous, it may be any or all of these, but this, I believe, is the exception not the rule. Let's be realistic and look at advertising for what it really is. In truth, it is one form of selling, it is educational, it is a particularly adaptable mode of fast communication. Certainly it has a purpose—to sell—but before one can sell anything, there must first be some form of communication which transmits information and thereby leads to education. Advertising is, without doubt, an essential and integral part of our free enterprise system—a system remember, which has brought more of the good things in life to more people in this country than ever before in all of the history of the world.

Scientific and Technical Information

Let me make myself clear on one point, however. I fully appreciate your desire to obtain, in addition to advertising, as much scientific and technical product information as is feasible. You need it for your pharmacy and therapeutics committees, you need it so that you can answer queries from attending physicians as well as the house staff, and you need it for your own professional activities in the pharmacy. To my knowledge, at least one major firm makes a concerted effort to supply you with adequate basic information about new drugs and new products.

It seems to me that the members of the American Society of Hospital Pharmacists could make their wishes and their needs clearly known to the drug industry. I see no reason, for example, why you should not be furnished with the 'professional brochure' for each new product. By 'professional brochure' I am referring to the brochure which the firm had to prepare and submit to the Food and Drug Administration as part of its new drug application. Many companies reprint this information and supply it to physicians as a basic medical brochure or professional brochure. It contains information on the chemistry, physiology, pharmacology, indications for use, contraindications and side effects, and dosage directions. This is authoritative information which has been reviewed in detail by FDA. In my opinion, it will serve your purposes quite admirably under most all circumstances. If and when special questions arise, you can, of course, seek additional information directly from the manufacturer of the drug, or enlist his aid in finding the answer if such is not immediately available.

Misuses of Hospital Formularies

And now I would like to turn to the rather lively subject of hospital formularies. You use them on a daily basis and are intimately familiar with their workings. I, too, have been exposed to their workings in several different capacities—as a physician, as a government official, and as a representative of the drug industry. Hospital formularies, in my mind, definitely serve a useful purpose. Unfortunately, however, in some instances I believe they are misused, if not abused. Let me elaborate by telling you what I think a formulary should not be and should not do.

First and foremost, a hospital formulary should never, and I repeat never, be allowed to interfere with, delay, or otherwise impede patient care.

Secondly, the hospital formulary must not be permitted to usurp either the legal or professional preroga-

tives of duly licensed physicians. Believe me when I say this is a step in the wrong direction which can easily lead down the road to socialized medicine. Regimentation must not be confused with orderliness.

Thirdly, the hospital formulary must not be an excuse for the purchase of junk—inferior products if you will. Relatively few hospitals in my experience have adequate laboratory facilities or competent people for quality control. Yet I am repeatedly amazed at the widespread purchase of off-brand merchandise without real knowledge of the integrity and reputation of the manufacturer. The naive belief that if the product was not good, the Food and Drug Administration would prohibit its sale is just not realistic. FDA labors long and diligently to protect the public, but the fact of the matter is that it is completely impossible for FDA to check every batch of every product of every manufacturer that is marketed. Hence, the integrity and reputation of the manufacturer assumes unusual significance where drugs and health products are concerned.

Fourthly, the hospital formulary should not be a fulcrum for price manipulation. I am aware that the pharmacy is one of the three money making departments in most hospitals and that you receive some pressure from hospital administrators to help decrease the overall operating deficit. I am appreciative of this situation, but nonetheless, I don't believe that quality should be sacrificed for price.

Duplication and Imitation

You as pharmacists are all familiar with the fact that some companies seem to specialize in duplicating and imitating reputable and useful products. Surely, they can undersell the firm who originally developed the product. After all, they had none of the research costs to bear, none of the costs of promotion and professional education. In essence, they walk into a ready-made market. They have contributed absolutely nothing to your profession or to mine. Surely, their companies can imitate good products, surely, the price is attractive, but how do you know you are getting good quality or full labeled potency? I know of cases where this kind of firm purposely included only 75 or 80 percent of labeled potency. Subpotent yes, illegal yes, but often extremely difficult to detect clinically. All such instances should be reported immediately to the Food and Drug Administration, but how can you, the pharmacist, tell unless you run your own quality control? The answer is in most instances, you can't; but when this does happen, you, your hospital, and the patient are all being cheated.

Granted there is much merit in 'the lowest bid philosophy.' The taxpayer, and I am one, is entitled to have his money spent honestly, carefully, and economically. Let me hasten to add, however, that the sacrifice of quality and reliability for price is indeed false economy. Worse, if the patient suffers as a result, it is criminal.

Let me return to my title. The hospital formulary

is really "just a little piece of paper," but look at its tremendous ramifications and responsibility. Look at the way it directly affects human life.

What Formulary Should Be

So far I have expressed my views in the negative. Now let me tell you briefly what ideally, I believe, the hospital formulary should be. It is truly an educational tool for the entire hospital team. It should be a critical reflection of the current thinking of the best informed physicians on the hospital staff concerning the use of drugs. It should be oriented in terms of science, therefore *a priori* objective, and in terms of what is best for sick people. A formulary, any formulary, must always provide latitude for the physician, legally and morally charged with the ultimate responsibility for the patient, to order any drug at any time that he believes is in the patient's best interest—yes, even if the patient dies, and even if the physician is wrong in his choice of drugs.

I don't know that I have adequately described or defined the functions of a hospital formulary. I have, however, expressed my own views as a physician. Let me repeat, I endorse the principles of a formulary, but it must be a constructive instrument of service not an impediment to progress or to patient care. To sum this up, in my judgement, the doctors must control the formulary, the formulary must not ever be allowed to control the doctors.

Opportunities for Professional Practice

There are many areas where the hospital pharmacist is and can be increasingly important. For example, in the March 1959 issue of *New Medical Materia,* an excellent new medical publication by the way, they report that based on a survey of 4200 physicians only 6.4 percent indicated they obtained their first knowledge of a new drug product from the hospital. I think you can improve this figure, to your own credit and to the benefit of medicine and pharmacy in general. You sit right at the heart of what is probably the fastest growing field of pharmacy. To illustrate, in the August 1959 issue of *New Medical Materia,* they report that the number of annual admissions per hospital has increased from less than 2500 in 1953 to 3500 in 1958. This, despite a decline in the number of hospitals of 192 during the same period, obviously means you are busier. Coupled with the rapid rate of new drug development, this gives you almost unlimited opportunity for the exercise of your professional knowledge and know-how.

You and I are happily associated with the one industry that spends more research dollars as a percentage of sales, that is, has the highest ratio, than any other industry in the entire United States. In the April 1959 issue of *New Medical Materia* you will find that the ethical drug industry spent 6.5 percent of its sales dollars in 1958 on research, whereas the chemical industry by comparison spent 2.6 percent, aircraft 1.4 percent and the petroleum industry only 0.7 percent. I don't know how it makes you feel, but I am proud to be associated with a profession and an industry dedicated to health, the relief of pain and suffering and an industry which does more than just pay lip service to its cause—it spends hard earned dollars for its future and our future—yours and mine.

And now before closing, a few miscellaneous thoughts for your consideration. We are all aware of the great international tensions that exist. Hopefully they can be resolved peaceably. In the interim, however, it is our civic and professional responsibility to be prepared in the event of emergency. Quite apart from warfare, any of us might be subjected to disaster conditions on a regional or community basis at any time. It is in our own self-interest to be prepared. I think you should look forward to the day when, in the event of emergency, the hospital pharmacist could be called into service to render emergency care directly to patients. Each hospital should have well integrated disaster plans in which the pharmacist may have to delegate his dispensing activities to a trusted and pretrained assistant and devote his efforts to the immediate saving of life.

You, as a group, under the leadership of the American Society of Hospital Pharmacists should offer your organized help to the medical staff of your hospital. Likewise, as a Society you should offer your help to appropriate Civil Defense authorities. I feel certain they will welcome your cooperation and support.

Recently I have had occasion to review your annual membership list as published in the American Journal of Hospital Pharmacy. In its present form, giving home addresses, I'm sure it is very helpful to you. I believe its utility could be increased, however, to everyone's mutual advantage if the hospital affiliation of each member were also recorded when known. I have never been impressed with the wisdom of addressing mail to the chief pharmacist of such and such a hospital, or to the chief of the medical service. Some of your members have discussed with me the desirability of receiving more informative and descriptive literature from the drug industry. Why not make it easy for industry to send it and easy for you to receive it. To my knowledge, there is no entirely satisfactory list now available except in the hands of a few companies who have been enterprising enough to compile their own. You could easily remedy this situation.

And now may I express my appreciation for the opportunity of participating in this meeting and appearing on your program. Let us not forget we are engaged by choice in the business of saving lives. A chart order, a written prescription, the hospital formulary, yes even a drug purchase order can sometimes mean the difference between life and death. Each is equally important. Each is "just a little piece of paper."

packaging of OPHTHALMIC PREPARATIONS

by SISTER MARY FLORENTINE

► WHEN SCANNING THE LITERATURE ON THIS subject for the past decade, one finds it evident that while much concern has been evidenced in the matter of preparing ophthalmic solutions in a manner to ensure their sterility, the container itself has received but scant attention. In fact, there has been little departure from the long accepted concept of a container for collyria, until the advent of the various forms of plastic containers and dropping devices, and disposable units of all kinds. The ophthalmologist wishes drops to be placed both in eyes which are intact and in those in which the natural protective barrier has been broken, either by accident or surgical intent. How these drops are to be dispensed rests in great measure with the compounder and dispenser. Here we have a wide field for service and adaptation of our particular fields of knowledge and skill.

The packaging industry today is tremendous and eagerly in search for new uses for their products. We must be ready to take advantage of these advances, or we will find that we are rapidly being left behind.

SISTER MARY FLORENTINE is Chief Pharmacist at Mount Carmel Hospital, Columbus, Ohio.

Presented at the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, August 17, 1959, Cincinnati, Ohio.

Once again, we will find commercial interests reaping the benefits of our pioneer endeavors.

Problem of Small Containers

Looking back some twenty-five years, I recall that while I was in a children's hospital with a moderately large outpatient eye service, the problem of dispensing in small containers, because of the nature of ophthalmic drugs, first occupied my attention. I must confess that at that time, however, my chief concern was amounts of alkaloidal materials used at home for preparation for refraction which could be left around with danger of misuse. So rather crudely, as I now see it, we dispensed these drops in half-dram homeopathic vials with a separate dropper wrapped in paper. In those days there was not so much concern either pharmaceutically or ophthalmologically about the sterility, or isotonicity of the preparation—distilled water, perhaps filtered through cotton if any microscopic particles were visible. A far cry indeed from our elaborate techniques today.

Well known in this era were the ground-glass stoppered bottles used extensively for stains, usually holding an ounce or more, which were a familiar part of every treatment tray. The standard prescription type dropper bottle also could be obtained in half ounce sizes as well as larger ones. Once a month seemed sufficiently often to remove the accumulated seaweed from these containers, and we were very scrupulous on this point. Do I note a shudder? Well, ignorance is bliss and the age of sterility was yet to come. In 1945 *The Bulletin*[1] discussed the system in use at the University of Michigan. This employed ⅛ ounce dropper bottles ("Moderne" obtainable from Pennsylvania Glass Products) which contained "4 c.c., sufficient to last the nursing units for a week." This was a great improvement except for the difficulty of cleaning the small units and sterilizing them, but nothing in comparison to the next method which was brought back to us by one of our young physicians who had trained in New York. This unit, similar to the packages of sensitivity-testing material formerly packaged in some antitoxins, consisted of a 1 c.c. vial, a capillary tube, and a rubber bulb. Through the courtesy of one of the manufacturers of antitoxins, we were supplied with a quantity of these units. The cleaning and preparation steps with these units were extremely arduous and we soon returned to the Moderne type. These were in use with many variations in buffering, non-buffering, use of preservatives or not, with general satisfaction, barring a few exceptions, on the part of the clinicians for nearly ten years.

Polyethylene Dropper Units

The use of polyethylene dropper units was discussed in *The Bulletin* in 1954.[4] The first units made available by Plax were sealed at the lower end and filled either by expelling the air from the container and sucking in the solution or filling with a needle through the top opening. The disadvantage here was that the containers could not be sterilized by the ordinary methods available in hospitals, and had to be soaked in benzalkonium solution. In most cases this did not matter since it was the ordinary vehicle for the solutions themselves, although in the case of certain salts, notably pilocarpine nitrate and physostigmine salicylate, there was a chemical incompatibility. For a year or so this technique served admirably, then the manufacturer ceased making the units and the search was on for a new type of container.

Bracon Plastic Tubes

Late in 1954 *Modern Packaging* discussed such a unit, the Bracon type, made by the Bradley Container Corporation. After an effort on Bradley's part to steer our small order toward "Iso-Sol" a manufacturer of ophthalmics, (their reaction being that they would be delighted to furnish us with their own product) we were finally able to secure the small units with a blind tip. Thus in 1955 we converted our entire ophthalmological line to these tubes; our own solutions as well as those purchased from other sources. After the usual growing pains it was very well received and became an accepted procedure. However, the growth of Bradley and two passages of the company from one large corporation to another soon left us in the position that any order for less than 50,000 tubes would not be considered. Threats, cajolings were to no avail. Moreover, no longer could Bradley supply them in a sterile condition, having disposed of their high voltage equipment. So the very satisfactory situation must needs be amended. Now we have enough tubes for several months but then a change is again in the offing. We face this with regret. Why? Because the tubes were used as well for packaging small units of ointments, even breaking down the usual 4 dram tin tubes to smaller ones for economy where the clinician wishes to use the tube but once and then discard it. The system has worked admirably in our situation and we regret the possible discontinuance without some suitable replacement. At one time Bradley was trying to interest some distributor of hospital supplies in jobbing their units in smaller lots than their 50,000 minimum, but apparently this has never come to fruition.

The Wheaton Company with conscious approach to hospital needs now has made available a line of polyethylene dropper units which can be purchased sterile in plastic bags. However, their smallest unit is ¼ ounce and the problem of wastage of expensive materials is therefore attendant upon their use. For outpatient dispensing they are, of course, ideal and

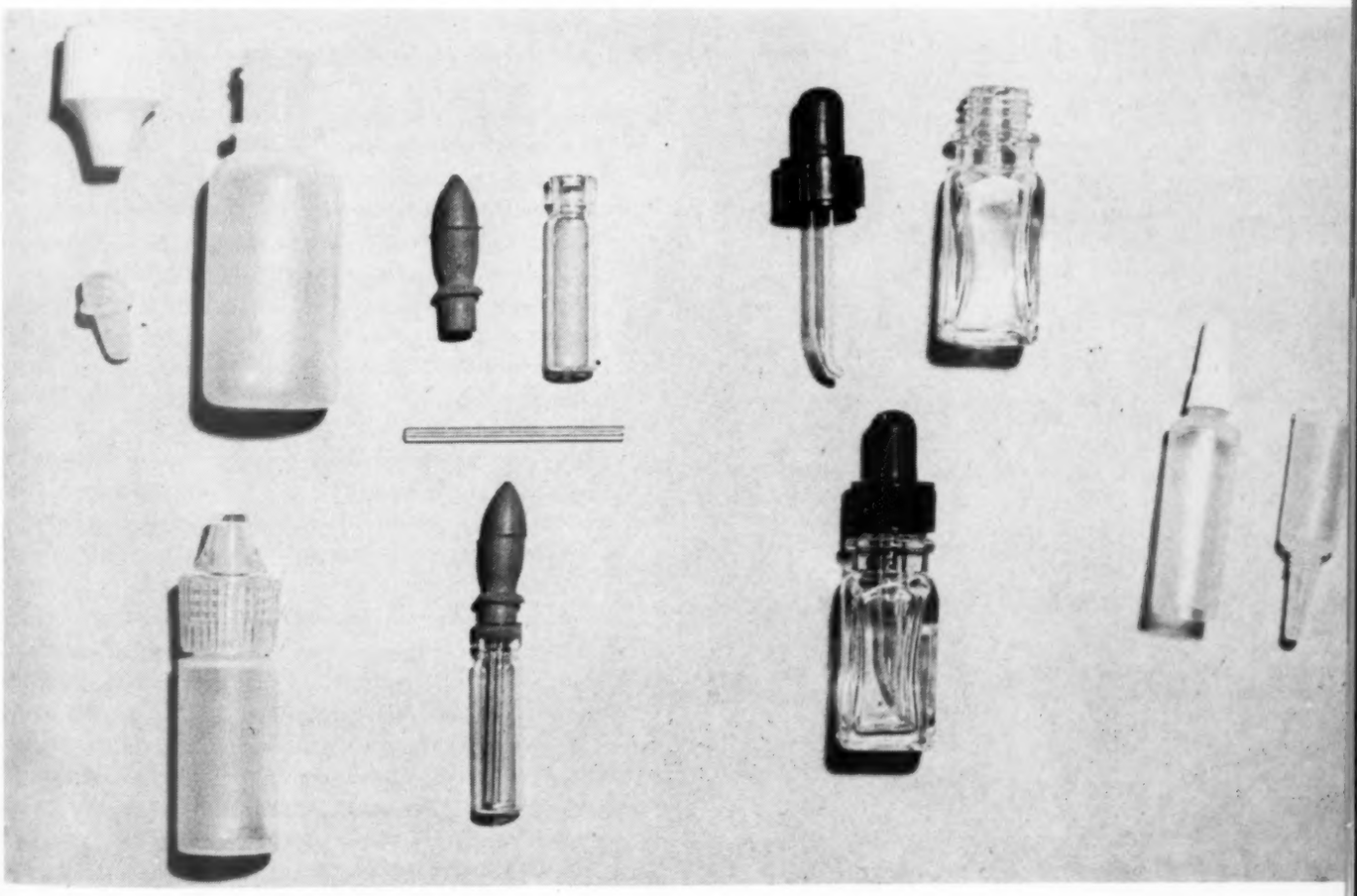
Wheaton is to be congratulated for being so cognizant of the needs in this field.

Ophthalmic Ointment Containers

Before returning to the discussion of yet another type of plastic unit, I should like to introduce the subject of containers for ophthalmic ointments. Here, too, we have assumed for many years that ointments could not possibly be harborers of micro-organisms, only to have our complacency shattered by the findings of researchers. Commercially available units were found to have high bacterial populations, many formulations still in demand have been deleted. The obvious solution, in line with the home refurnishing market, was—"Do it yourself." Standard ophthalmic tubes are available from several sources, some in reasonable amounts and others in carload lots only. The sterilization and preparation of such units can quite simply be undertaken in any hospital pharmacy. This is time-consuming, yes, but a valuable service, which is most certainly what we wish to give. The small Bracon plastic tubes serve well here. In our own hospital we use them for small amounts of expensive ointments for the treatment rooms where one application is made and the tube discarded. A fascination for disposable units, paralleling Mr. Bogash's, would lead us to point out the practicability of a small sealed foil unit similar to those now being used as samples by many of the pharmaceutical houses. Perhaps his fabulous machine will do even this along with cream and butter-pats and pills and cough syrups, and I envy him. Such foil units are offered by contract packagers and, perhaps in larger hospitals with a great volume, even this might be feasible. During the past year many of you perhaps saw a very tiny tin tube used by the Upjohn Company for sampling steroid ointments. Repeated requests of collapsible tube manufacturers only elicited the response that this had been a special job for the company and they had no intention at this time of going into routine production of such small units. Perhaps our united efforts could cause them to reconsider, for it seems that the 1 gram unit would be ideal.

Another approach, also by Upjohn, and available for a while to anyone interested in buying them, were the sealed, electron beam sterilized gelatin "Escaps." We found them extremely useful especially in the nurseries. Again the economic factor caused Upjohn

LEFT TO RIGHT: *Wheaton plastic unit; Dropule unit, Pennsylvania Glass Company "Moderne" one-dram; Bracon tube, 1 ml.*



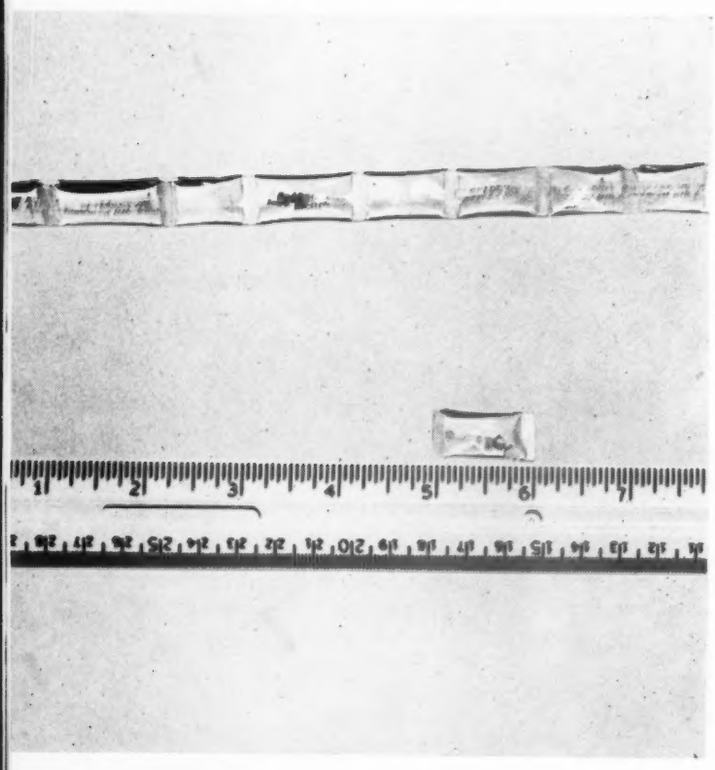
to delete this item. Personally, I feel that this is a great loss since this unit seemed to approach most nearly to the ideal.

Ideal Ophthalmic Solution

What then is the ideal? Skolaut[2] has suggested that the ideal ophthalmic should be: (1) Free from microorganisms and should remain so after a reasonable length of time, (2) should be nonirritating, (3) should be stable, (4) should have optimum activity. Riegelman and Vaughn[19] go a step further and suggest a "single-patient container autoclaved 15 minutes at 15 pounds." These requirements are obtainable in any hospital pharmacy and Murphy has outlined equipment and appended prices for a set-up practical for any pharmacy.[11]

The problem of buffering and non-buffering, preservatives *vs.* autoclaving, has received much attention, and it seems that the system to adopt is the one best suited to your own particular circumstances followed with care and frequent checks to see that the system adopted is functioning as well as hoped.

Sterile sealed units in Kel-F Plastic tubing



Advantages and Disadvantages

All the containers discussed in the preceding paragraphs have some kind of drawback. We are creatures of habit most truly and our minds and thinking are circumscribed by tradition and habit. To change the form, or size of the container takes perseverance, discussion with physician, patient, and above all the nurses who will be the intermediaries between the pharmacy and the patient. They can make or break the best hoped-for program. Because everyone is accustomed to dropper bottles, smaller versions of standard dropper units are the logical step to individual containers. The disadvantages encountered here are primarily in your own department: they are tedious to clean, assemble and fill. Since they are made of soft glass there is some leaching, with subsequent change in *p*H upon autoclaving.[11] They are the most conformable to accepted patterns of habit, low in cost, conform to U.S.P. standards for containers, and can be readily sterilized either by steam or dry heat.

The Bracon plastic tubes made of polyethylene have the disadvantages of that material. The chief drawback has been the tendency of the tubes to act as a semipermeable membrane, causing oxygen transference and loss of water with attendant changes in concentration. Newer tubes are being internally coated to prevent this fault, although there is still considerable water passage at ordinary storage temperatures. This can be obviated to a great extent by storage in the refrigerator. Polyethylene is soft, and cannot be sterilized by heat, although the newer high density grades of polyethylene are firmer, and in several instances are heat sterilizable. There are several features of Bracon tubes which are valuable for the packaging of ophthalmics to be maintained in a sterile condition: (1) they may be purchased with a "blind tip" so that the tube when filled with sterile material and sealed at the bottom will be essentially a hermetic container. There are also tips which will release only one drop at a time, and for ointments the "suck-back" advantage and the fact that the tube does not become distorted are valuable features.[20] Those that currently are being produced can be sterilized only by ethylene oxide, electron bombardment, or chemically; but with rapid advancements in the plastics field it is hoped that the company will adopt some of the newer materials for these tubes. Another bad feature is the very large orders required, the minimum order being for 50,000 tubes.

The T. C. Wheaton plastic containers are available in various sizes, from ¼ ounce up, either sterile or non-sterile and this feature, except for the larger sizes would make them practically ideal. The observations of several investigators on the suitability of plastics for pharmaceuticals stress the passage of gases, as well as water vapor, and it is believed that especially in the case of carbon dioxide "may change

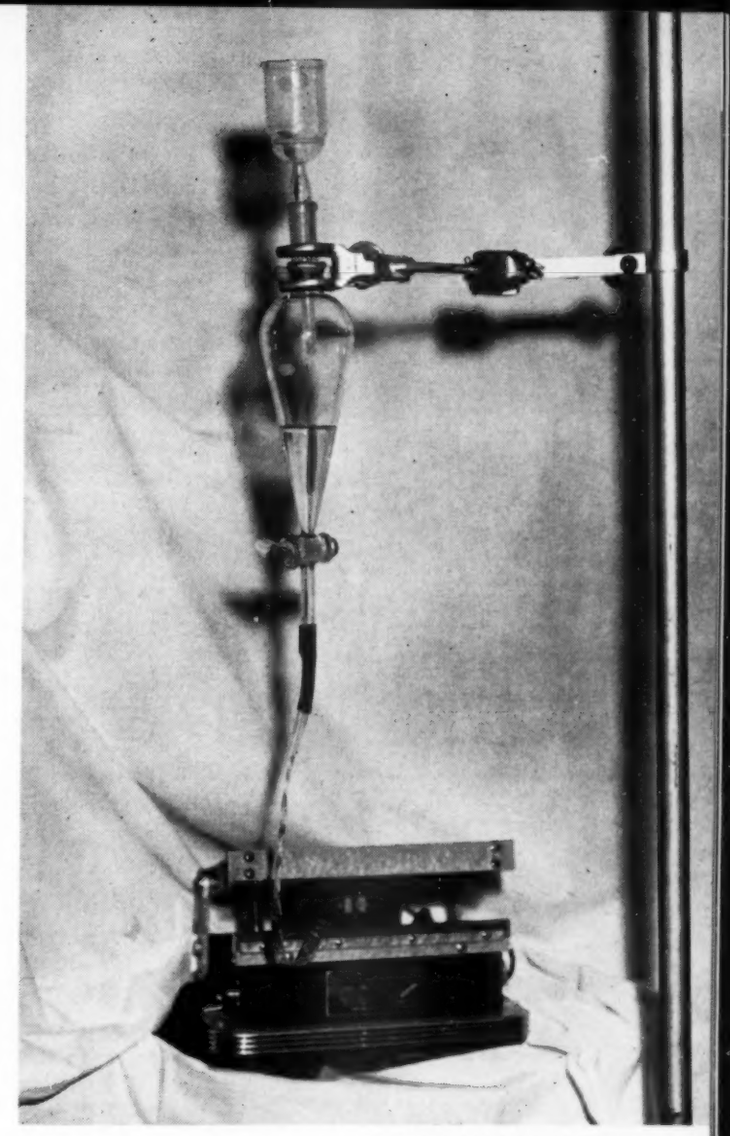
the *p*H sufficiently to cause precipitation of weak bases." There is always the problem of patient acceptance of new containers, but the many features such as being light, easy to carry in purse or pocket, unbreakable as well as leakproof, soon sell themselves.

Economic Factors

The economic factor in all of this discussion is of vital interest to you all. In our own particular case, although we do not have accurate cost accounting and have not broken down time factors in arriving at the figure, we estimate that a sealed sterile, plastic unit of atropine sulfate 1 percent costs between 5 and 6 cents. This unit cost will vary with the more expensive preparations but remains merely an additive factor, and when considering the savings on wastage in expensive items, well worth the trouble. I know of one large tax-supported institution where, even with the buying advantage prevailing, it was estimated upon adoption of a commerical system of ophthalmic preparations that the original three-months' inventory was approximately $2,000. I cannot believe that the trouble involved in preparation of such units would not be worth such an obvious economic advantage.

Storage Problems

Several years ago a chance remark by one of our ophthalmologists started me in pursuit of what, up to now, has been a chimera. But I am quite sure the problem can be solved; we have already overcome several obstacles, and, as is usually the way, a commercial version is already on the market. That idea was simple, "Why not a disposable unit similar to the wax silver nitrate ampuls?" My thinking then went to plastic and a tubing sealed off at intervals, a string of sterile sausages so to speak. It sounded simple, and probably would be to one with all the technical knowledge needed, as I was soon to learn, for since February of 1956 I have pursued this elusive bit of simplicity, beginning with a patent search with a friend who thought that there might be a commerical possibility. So it was soon discovered that the new idea was covered pretty well by ideas already registered and dating back for a period of ten years. That spring and early summer were devoted to preparing a limited number of units using heat sterilizable intravenous tubing sealed on a sealer loaned to us. This sealer, as anyone could tell who saw my demonstration at the Chicago Institute in 1956 on machines that wouldn't work, was not suited to this particular technique. One session with fluorescein convinced me that the machine should be returned to its owner! Studies that summer demonstrated that polyethylene tubing was not ideal because of the rapid water loss at room temperature. We found that a month's stor-



Sterile ophthalmic filtration (closed system) with foot operated heat sealer for plastic tubing

age under these conditions was sufficient to cause a complete loss of contents. Storage in the refrigerator retarded this loss almost completely. Since this is a weakness of all soft polyethylene containers we have continued the practice of storing our eye solutions in the refrigerator. This also cuts down deterioration of the alkaloidal salts. We have three tubes of our original experimental material which have been stored under refrigeration for three years, and even so have lost about 50 percent of their original content. This lengthy period is, of course, an extreme case and would not be met with under ordinary circumstances. At room temperature we have found that solutions stored in polyethylene bottles, lose approximately 2.5 percent of their total weight per month. We have not done any studies on the newer coated containers, relying solely on the storage conditions and rapid turnover.

New Plastics

About a year ago we renewed our interest in the problem by trying to adapt the remarkable properties of Kel-F plastic to this particular usage. This material is clearer, considerably stiffer, and is sterilizable with steam under pressure. How I envy places with research staffs, and secretaries! For over a year we have been writing back and forth between the manufacturers of tubing, and those who supply sealers for this type of material. One company avowed themselves most happy to help if they only knew what kind of *sealer* we would use, while sealing machines could be furnished only if we would tell the kind of *tubing* to be used! While all this exchange was helping the postal authorities to balance their budget, a unit became available from Barnes-Hind using this material, and in the form we had been seeking. To date, however, they do not have a complete line and the price per unit is still considerably too high for general usage. We've all had the experience of seeing something new and wishing that we had thought of it first, but to have thought of it and see someone else come along first is discomfiting to say the least.

The future seems to hold much promise, however. Aside from the Kel-F plastics, there is new Hi-D (high density) polyethylene which is also heat sterilizable. A small ethylene oxide sterilizer has become available in which small amounts of heat sensitive plastics may be sterilized so lower melting polyethylene tubing may be utilized. This material may be readily marked with a rubber stamp and special plastic stamping ink. So it seems that with a minimum of expense a hospital pharmacist may readily prepare sterile disposable units of ophthalmic solutions at a price considerably below that for commercially available ones. This technique will give a complete range of solutions desired in any institution since any desired solution or strength can be prepared once the technique has been adopted. This, I believe, is a great advantage over any of the available units from commercial sources, no one of which has an entire range of alkaloids or percentages. If I have given an incentive to a few more searchers for a system, please let me know about your experiences. They can be fruitful as well as frustrating.

Bibliography

1. Notes and Suggestions, *Bull. Am. Soc. Hosp. Pharm. 2*:147 (Sept.-Oct.) 1945.

2. Skolaut, Milton: Ophthalmic Medications, *Bull. Am. Soc. Hosp. Pharm. 5*:172 (July-Aug.) 1948.

3. Cataline, D.: Preparation of Eye Solutions, *Bull. Am. Soc. Hosp. Pharm. 7*:264 (Sept.-Oct.) 1950.

4. Wai, Y. Wu and Job, Betty K.: Polyethylene Tubes for Eye Solutions, *Bull. Am. Soc. Hosp. Pharm. 11*:42 (Jan.-Feb.) 1954.

5. Altbach, H. and Mazzapica, F.: Ophthalmic Solutions—A Report on the Sterile Manufacture of Them, *Bull. Am. Soc. Hosp. Pharm. 12*:456 (July-Aug.) 1955.

6. Weil, Lillie: Simplifying the Dispensing of Sterile Fluorescein, *Bull. Am. Soc. Hosp. Pharm. 13*:62 (Jan.-Feb.) 1956.

7. Webb, John and Haye, C. V.: Combining the Effects of Cobalt-60 and Chlorobutanol for Sterilizing Ophthalmic Solutions, *Bull. Am. Soc. Hosp. Pharm. 13*:466 (Sept.-Oct.) 1956.

8. Goettsch: Sterility of Eye Drops (abstr.), *Bull. Am. Soc. Hosp. Pharm. 14*:697 (Nov.-Dec.) 1957.

9. Archambault, George F.: Plastics and the U.S.P. Requirements for Tight, Light-Resistant Containers, *Am. J. Hosp. Pharm. 15*:877 (Oct.) 1958.

10. Webb, J.: Preparation of Ophthalmic Solutions, *Am. J. Hosp. Pharm. 16*:164 (Apr.) 1959.

11. Murphy, Allen and Mangiaricini: Preparation, Sterilization and Preservation of Ophthalmic Solutions, *Arch. Ophthalmol. 53*:63 (Jan.) 1955.

12. Lawrence, C. A.: An Evaluation of Chemical Preservatives for Ophthalmic Solutions, *J. Am. Pharm. Assoc., Sci. Ed. 44*:457 (Aug.) 1955.

13. Vaughn, D. J., Jr.: The Contamination of Fluorescine Sodium Solutions with Special Reference to Pseudomonas Aerug., *Am. J. Ophth. 39*:55, 1955.

14. Theodore, F. H.: Contamination of Eye Solutions, *Am. J. Ophth. 35*:176 (May) 1952.

15. Theodore, F. H. and Feinstein, R.: Practical Suggestions for Preparing and Maintaining Sterile Ophthalmic Solutions, *Am. J. Ophth. 35*:656 (May) 1952.

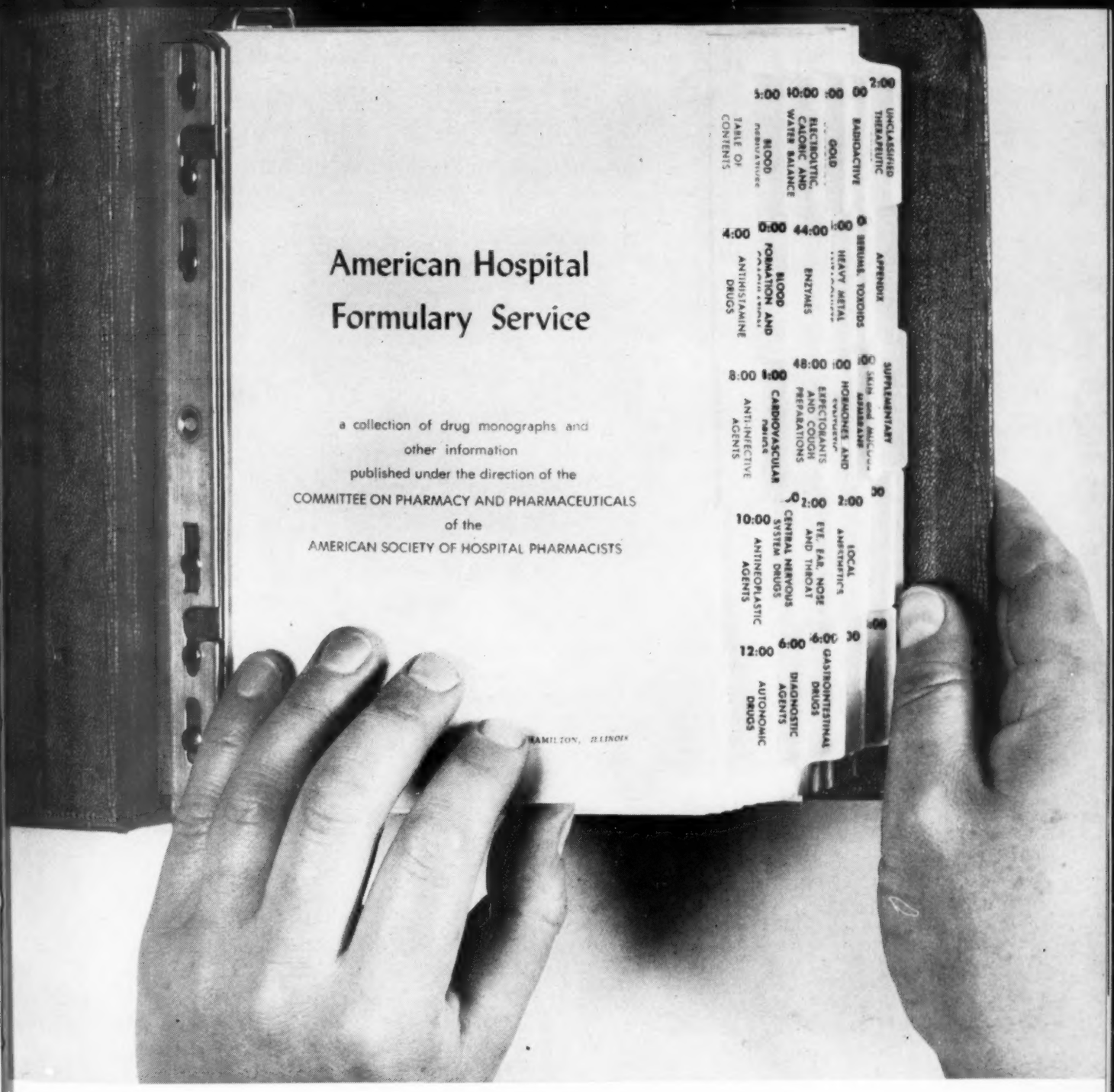
16. Lawrence, C. A.: Chemical Preservation of Ophthalmic Solutions, *Am. J. Ophth. 39*:385 (Mar.) 1955.

17. Riegelman, S., Vaughn, D. G. Jr., and Osumoto, M.: Rate of Sterilization as a Factor in the Selection of Ophthalmic Solutions, *Arch. Ophth. 54*:725 (Nov.) 1955.

18. Autian, J.: The Effects of Plastics on Parenteral Products, *Bull. Parenteral Drug Assoc. 11*:25, 1957.

19. Riegelman, S. and Vaughn, D. J.: Rational Basis for the Preparation of Ophthalmic Solutions, *Am. Profess. Pharmacist 24*:757 (Oct.) 1958.

20. *Bracon Fact Sheet*, Bradley Container Corp., Maynard, Mass.



CURRENT STATUS OF THE AMERICAN HOSPITAL FORMULARY SERVICE

by WILLIAM M. HELLER

► SINCE I LAST REPORTED to this House of Delegates 16 months ago in Los Angeles, a lot of Mississippi River has spilled over the dam above Hamilton, Illinois, and a lot of pi has accumulated on the east bank on the floor of The Hamilton Press.

Only the day before I last spoke to you did we finally set a target date for the initial publication. We did not meet it. We still shudder when we think about it. We regret the considerable inconvenience which our delay in publication caused many of you.

I recall this unwanted memory to mind only to give due recognition to four members of the SOCIETY who got us out of our dilemma: Mrs. Gloria Francke, our Secretary; Mr. Paul Parker, Director of the Division of Hospital Pharmacy; Miss Joanne Branson, a pharmacist at the University of Michigan Hospital; and George Provost, then a pharmacist at the University of Arkansas Hospital. These people spent two to four weeks each at The Hamilton Press getting the type put to bed. Their job was to correct, and correct, day and night, until every page was perfect. That they did an excellent job is attested by the paucity of errors called to our attention.

The initial publication was distributed during the latter part of January and early in February. Even before it was in the mail, a second printing two and one-half times as large as the first was ordered. Still it could not be prepared quickly enough and once again we were out of Formularies. The second printing became available the first of July and all outstanding orders have been filled.

All this was done with comparatively little monetary investment from the SOCIETY. In this respect we are indebted to The Hamilton Press for their confidence in our undertaking. The initial risk is no longer a risk. We are now a successful operation and are already self-supporting. And it has become too big an operation to handle satisfactorily with largely voluntary help.

Future Plans

Meeting in Memphis in the latter part of May, four months after the first copies of the Formulary were distributed, the Committee on Pharmacy and Pharmaceuticals reviewed our position and charted our course for the near future, at least.

The Committee recommended the employment of a full-time pharmacist to assist the chairman and to relieve the Secretary of the SOCIETY of many of the routine duties concerning the Formulary Service which she had handled through her office. With the appointment of George Provost to this position on July 1st, we have secured a pharmacist who can not only handle the routine work but can contribute greatly to the preparation and revision of monographs.

One other person has also assumed the responsibility of initiating monographs—Mrs. Joy Blickmore Plein, Ph.D. Dr. Plein is associated with the University of Washington College of Pharmacy and teaches pharmacology in the school of nursing in a local hospital. Except for the replacement of Dr. W. Arthur Purdum by Clifton J. Latiolais, no other changes in the Committee on Pharmacy and Pharmaceuticals or its Reference Committee have been made this year.

We have had inquiries concerning the absence of physicians on our Committee, and your own physicians may wonder about this. The Formulary Service is the product of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. It was conceived and planned by members of this SOCIETY, sponsored officially as a SOCIETY service, and it is only natural that we would call on our own members to do the work.

Nevertheless, we do enlist the aid of persons of other professions. One of the advantages of having a committee composed of hospital pharmacists is that each of those pharmacists has access to specialists of many types in his hospital. The pharmacists on our Committee are expected to and do take advantage of their intimate professional association with members of other health professions in their institutions.

In addition, it is expected that a few physicians will be appointed to our Reference Committee in an official capacity. These members will be helpful in assuring that the terminology is current and that the content of the monographs is most useful to physicians. We already have a nurse on our Committee for the same reason in respect to the needs of nurses.

You are the people whom your staff will be questioning about the Formulary Service, so you should be familiar with the manner in which the Committee works.

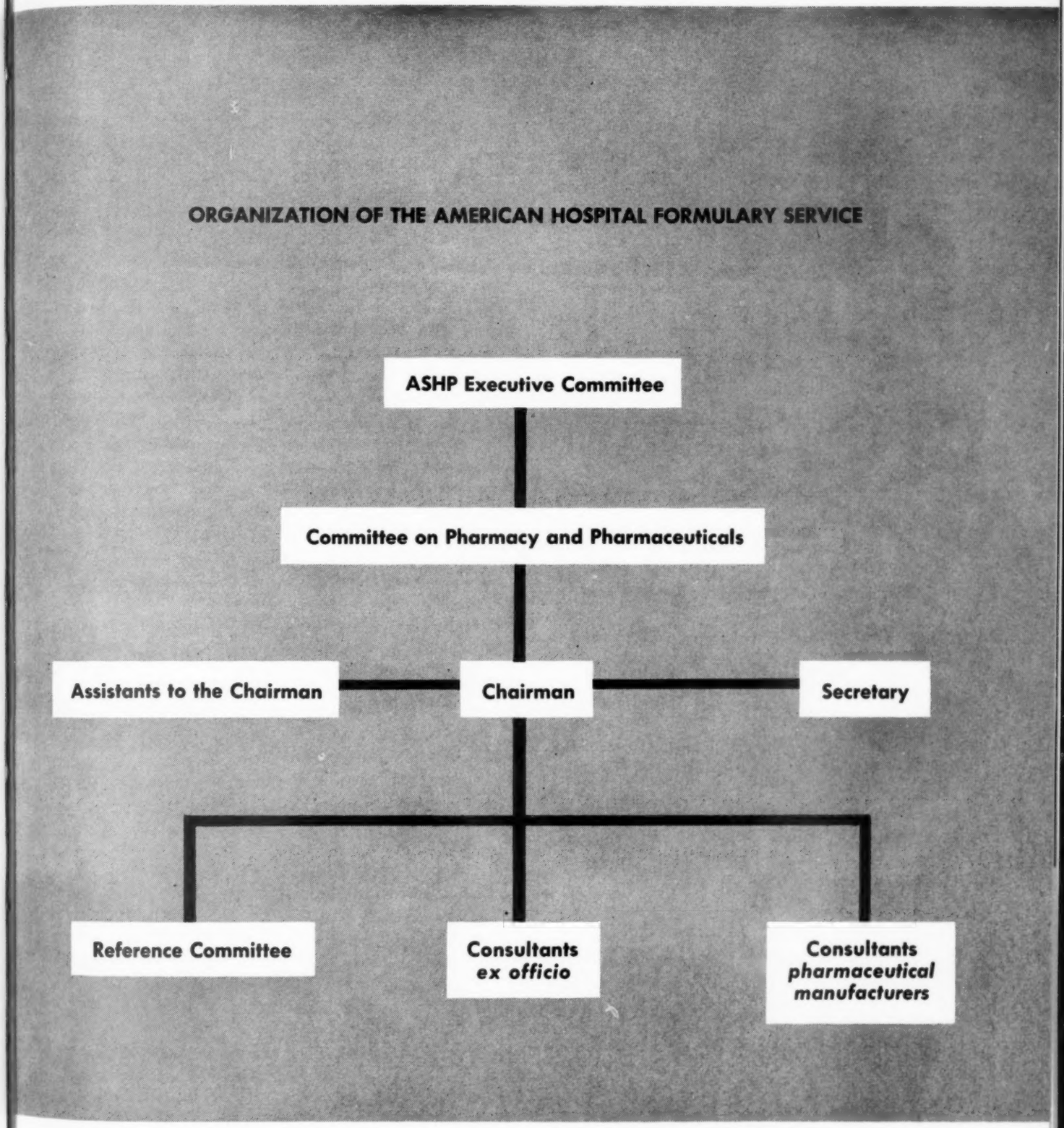
The Committee on Pharmacy and Pharmaceuticals is composed of five hospital pharmacists. This is the policy-making group. The Reference Committee of the Committee on Pharmacy and Pharmaceuticals consists of practitioners and educators of the other health professions, as well as hospital pharmacists.

Preparation of Monographs

Monographs are prepared initially by one of four persons, depending on the pharmacologic-therapeutic classification of the drug. These are the Director, the two Assistants to the Director, Dr. Marc Jordin and Dr. Joy Plein, and the Secretary, Mr. Provost. All of the initial drafts are edited by the Director so that the style will be consistent. The second draft is then distributed to the members of the Committee on Pharmacy and Pharmaceuticals and its Reference Committee and to an appointed person in each of the firms distributing the product. Suggestions and comments of these people are considered in preparing the third draft. If major changes are involved, the third draft is sent back to the reviewers. If changes are minor, they are made by the Director and the third

WILLIAM M. HELLER, Ph.D. is Director of the American Hospital Formulary Service, and Director of Pharmacy Service, University of Arkansas Medical Center, Little Rock, Arkansas.

Presented by George P. Provost, Secretary of the American Hospital Formulary Service, at the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, August 16, 1959, Cincinnati, Ohio.



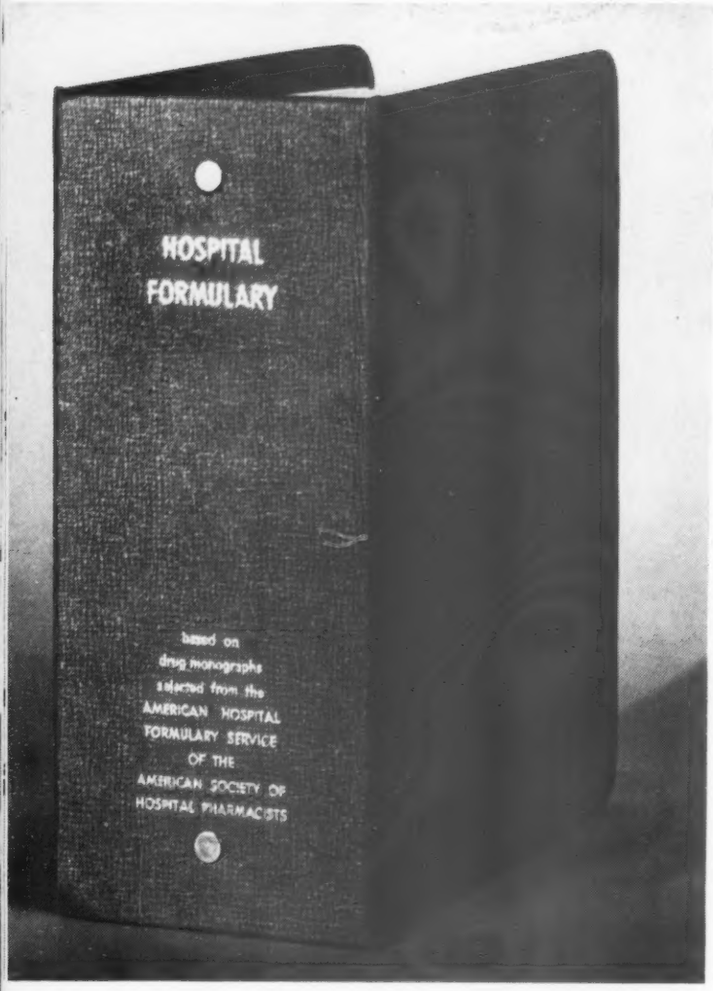
draft is set in type by the printer. Galley proof is sent to all reviewers for a last-minute check. From then on, it is the Secretary's job to work with the printer in correcting page proof and in grouping the pages and monographs to form a supplement of the proper size for the most efficient printing and distribution.

Obviously, this cannot be done overnight. As time goes by, we hope that both the Committee and the printer can decrease the time involved. As a check on the maximum speed we can attain under our present procedures, we suggest you watch for the monograph on griseofulvin. With good cooperation from the distributors and a fair amount of advance

reports on this drug, we were able to finish the first and second drafts a week after the drug was released.

We have been asked how we decide on which drugs to write monographs. Our Committee has a strong belief in, to borrow an analogy from the political world, "hospital rights." It is the responsibility of the Pharmacy and Therapeutics Committee of each hospital to decide which drugs will be included in its hospital formulary. Therefore, our policy is this: if the drug is likely to be included in many hospital formularies, a monograph should be available so that the drug may be used safely—regardless of the Committee's opinion of the merits of the drug. Since it is a practical impossibility to have a monograph on every drug, we are dependent on the Committee's opinion of which drugs are most likely to be included in hospital formularies. Subscribers can be of great help in this respect by keeping us informed of additions and deletions to their formularies. Why not put us on your mailing list to receive those announcements routinely?

A column in the AMERICAN JOURNAL OF HOSPITAL PHARMACY has been inaugurated as a means of communication between the Committee and the subscribers to the Formulary Service. In this column we will list the monographs under preparation so that in preparing your own monographs you may concentrate on those which will not soon be provided by the Formulary Service.



Uses of Formulary Service

The Committee recognizes that there are two uses of the Formulary Service: (1) as the basis for preparing a hospital formulary and (2) as a comparatively complete drug reference useful to practitioners and teachers in all the health professions concerned with drugs. To fulfill the former function, monographs need to be complete and accurate. To fulfill the latter, they need to be provided quickly. These two needs work against each other to an extent. Our general intent is to provide monographs as quickly as possible, then send out a revised monograph if later reports on the drug indicate a revision is necessary.

Since we are selling a service, not a book, we plan to send "change sheets" with minor information. From these change sheets you can make the minor changes in your formulary if you so desire and we will be providing our service in the most economical and efficient manner.

Unfortunately, as of today, we do not know all of the costs involved in the first and second printings and the first supplement. The Committee believes we should provide at least four supplements annually, and more if possible and necessary. I believe the necessity is there and that it will be possible to provide six or seven supplements within the next year. At

this time we have completed the first draft, at least, of 67 additional monographs. The second supplement is scheduled for distribution by the first of next month.

The price of the supplements was confirmed by the Committee at $5.00 per year. Quantity discounts will be available on the supplements as on the Formulary itself. Ten to 24 copies will be $4.75 each and orders for 25 or more copies will be $4.50 each. A card will be sent with the first supplement of the new subscription year. If the subscription is not to be renewed, the card is to be returned so stating. Otherwise, invoicing will be automatic. If you do not renew, the SOCIETY will have lost the cost of one batch of supplements. But we feel this is better than to delay the sending of supplements while waiting for you to renew your subscription.

There will come a point at which it will be more economical to incorporate the supplementary index into the main index than to continue reprinting the cumulative supplementary index each time a batch of supplements is printed. The number of books in our inventory will also be a factor. It is at this economic point, rather than at any particular time of the year, that we will distribute a complete new index and start over again with the supplementary index.

Despite the fact that new subscribers will receive all of the original material plus the supplements to the time their subscription begins and for the calendar year thereafter, the Committee has decided to maintain the initial price of the Service at $15.00 for another year.

There have been suggestions for the inclusion of more preparation formulas in AHFS monographs or for the publication of a separate bulk compounding compendium. Last year President Bogash appointed a special committee to study the feasibility of a bulk compounding compendium. The ASHP Secretary is reporting to you on the recommendation of that committee stating that a subcommittee on bulk compounding be set up by the Committee on Pharmacy and Pharmaceuticals. This subcommittee will invite research and reports in the following areas: (1) a definite formulation to meet an official specification; (2) a definite formulation to provide a nonofficial product; (3) starting formulations for nonofficial products; and (4) literature and opinion surveys of a general field of interest to bulk compounders: e.g., preservation of ophthalmic solutions; the use of bacterial filters; etc. It is expected that these reports will be printed in the AMERICAN JOURNAL OF HOSPITAL PHARMACY. Appropriate formulas will be taken from these reports and included in monographs in the American Hospital Formulary Service.

This Committee has provided and will continue to provide a great amount of material of value to you in the preparation of your own hospital's formulary. But you will note that we have not told you explicitly how to put it together or how to promote its use in your hospital. This is your responsibility. This goes with the "hospital rights" we mentioned previously. The SOCIETY is not supplying you with a hospital formulary. It is providing a service which will help you to provide a better and more complete formulary for your hospital than any of you is likely to prepare by yourself.

Still, it takes a lot of thought and time and effort to adapt this Service to fulfill in the best manner possible the needs of your hospital. We know that from experience. Mr. Provost has with him at this meeting the master copy of our own adaptation at the University of Arkansas Medical Center, together with our abridged edition. You may see these any time during the week. We encourage you to write to us of your own experiences and we will pass along through our column in the JOURNAL information which might be of value to other users of the Service.

The Pharmacist's Responsibilities

Any hospital can use the formulary system as a means of controlling drug costs and to enhance safety in the use of drugs through uniform terminology—and can accomplish these limited objectives with a simple drug list. But we earnestly submit that this is no longer sufficient. Drug therapy today is too complex for the average physician and the average nurse to keep up with all they need to know (and are legally responsible for knowing) in their hospital practice. Provision of this information on the actions, indications, dosage, and precautions in the use of drugs is the *greatest professional responsibility of today's practicing pharmacist*. The most effective and efficient way to accomplish this in the great majority of hospitals is to adapt to your needs the American Hospital Formulary Service. This will take work on your part. You should secure the necessary time and help for this function, just as you do for any other professional function for which you are responsible.

To those of you who have subscribed to one or two copies "to see how it looks," you have had time for appraisal. The Formulary Service is not perfect, but it is far superior to any other program generally available; and it will be constantly improving, as will your adaptation of it to suit your hospital's needs. You are now seven months behind the rest of us. With the annual meeting of our SOCIETY, we all renew our enthusiasm and begin a new professional year. Now is the time for action on your part. Now is the time to promote pharmacy and better drug therapy in your hospital by putting this Service to work. Now is the time—you, the pharmacist, will never know a better time—to become a more useful and necessary member of the patient care team.

Drug Cart showing the section housing the liquids and one of the metal storage cabinets. The opposite side is identical in construction, and houses the tablets. The pull-out drawer is on the right

experiences with a messenger service and drug cart in a general hospital

by BENJAMIN KAUFMAN *and* ISIDORE GREENBERG

► DURING THE SUMMER OF 1957 a broad study of the operational procedures of a hospital pharmacy was undertaken. Beth Israel Hospital is a general hospital of 367 beds and 54 bassinets, with an active outpatient clinic. It is located in a densely populated area of lower Manhattan, New York City. A specific assignment of this project was to study the character of the floor stocks with the object of standardizing them and, at the same time, to suggest procedures for improving distribution of drugs to the nursing stations.

The basis of this assignment was a general dissatisfaction with the drug distribution procedures at that time. Some of the factors making for this dissatisfaction included:

(1) Shortages arising after delivery of drugs to the floors necessitating the use of special messengers sent to the pharmacy to obtain emergency drug requirements;

(2) Extensive borrowing and exchanging of drugs between nursing stations;

(3) Accumulation of excessive and poorly arranged stocks of drugs at the nursing stations. Because of the latter, drugs could not be located when needed and the nurse requisitioned an "emergency" supply. This resulted in duplication which further compounded the problem;

(4) While there was a central emergency drug locker in the nursing office, its stock of drugs was inadequate both as to variety and quantity, and visits to the pharmacy by a nursing supervisor were required after the pharmacy closed for the night;

(5) Charges to patients for drugs were frequently overlooked; and

(6) The excess paper work and unnecessary detail which interfered with the primary functions of the nurse.

Establishment of Policy

With these considerations in mind, a series of meetings were held with representatives of administration, nursing, pharmacy committee, and accounting.

BENJAMIN KAUFMAN is Chief of Pharmacy Service, Beth Israel Hospital, New York, N. Y., and ISIDORE GREENBERG is Assistant Professor of Pharmacy Administration, Brooklyn College of Pharmacy, Brooklyn, N. Y.

Presented at the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, Cincinnati, Ohio, August, 1959.

This group proposed a set of principles embodied in a memorandum entitled: "Proposed Principles and Procedures Regarding Nursing Station Drug Stocks." Among the important elements in this memorandum were the following:

1. When finalized, this list of stock and emergency drugs is to be known as the "Standard Stock for Medical and Surgical Adult Nursing Care Units." It will be identical for all such units. Nothing is to be added to this list without the express permission of the Executive Director in concert with the Pharmacy Committee.

2. The proposed list of stock and emergency drugs must be considered from the point of view of completeness as well as the quantities indicated. Basic quantities should consist of a week's supply in order to minimize the frequency of replenishing.

3. The list should be classified according to the following categories: Barbiturates, Narcotics, Injectables, Tablets, Liquids, and others.

4. A copy of this list is to be affixed to the drug closet at the nursing stations.

5. This list of stock items constitutes free items that are administered to patients without charge. All other drugs, irrespective of their nature, must be ordered on individual patient drug slips regardless of whether ward, Blue Cross, private, or semi-private. Each of these drug slips must be priced by the pharmacy in accordance with a schedule to be later established.

6. Copies of each individual patient drug order slip whether ward, Blue Cross, private, or semi-private are to be sent to accounting, who will allocate to patient's card and determine who should be charged.

7. Charge drugs left over, due to physician's discontinuance or patient's discharge, will be routinely picked up from all floors and removed in an orderly

fashion, at least twice each week. The object of this is to prevent accumulation. This is in no way to be construed as relieving the nurses of their duty to return left-over drugs from patients who have been discharged.

8. A new requisition form, mimeographed, should be prepared for stock liquids. It should consist of the entire list together with the standard quantities. These orders shall be filled in the usual way, by tray or basket, at specified times which shall be established.

9. Barbiturates, narcotics, and tablet stock items can be replenished at the same time that left-over drugs are picked up with the aid of a specially prepared wagon containing sets of stock barbiturates, narcotics, and tablets. Provision must be made for obtaining narcotic requisitions and maintaining the perpetual inventory.

10. To facilitate the rapid filling of special drug orders, the following are required:

a. Extend the hours during which the pharmacy is open to 9:00 P.M., every day including Sunday.

b. Establish a messenger service and arrange for picking up orders and delivering drugs at two-hour intervals.

c. Augment the pharmacy personnel by an amount and type necessary to effectuate the increased hours and service.

d. Prepare a schedule of assignments for pharmacy personnel.

e. A careful inventory is to be made of the nursing office drug locker in order to stock it adequately for emergency orders between 9:00 P.M. and 8:30 A.M.

11. All affected personnel are to consider and devise operational procedures as well as educational campaigns necessary to bring these principles into operation by October 1, 1957.

Implementation of the Program

Meetings were held during the next few weeks, principally between nursing and pharmacy, to prepare lists and determine standard floor stocks for emergency and general use. After review by the medical and surgical services, the lists were approved. The drugs were grouped into four classes:

1. Emergency tray
2. Bulk preparations
3. General purpose floor stock
4. Emergency nursing office drug locker.

Emergency tray medications are maintained at predetermined stock levels by the nurse who requisitions new supplies immediately after using the quantity on hand. In the main, the items on the emergency tray are such drugs as must be ordered on an individual patient drug requisition as indicated above in item 5. The emergency tray is to be checked by the pharmacy at least once a month to assure that adequate quantities are on hand.

Bulk preparations, to be distributed without charge, consist of pharmaceuticals and other preparations in quantities of 32 fluidounces or greater. These items[1] are ordered on a replacement basis by checking off on a mimeographed list. Because of their bulkiness, they cannot be distributed from the Drug Cart, described below. Instead, twice each week, empty containers together with the requisition list are sent to the pharmacy, in a large drug box on casters. The containers are replenished or replaced and returned to the nursing unit.

The general purpose floor stock consists of drugs falling into the following categories:

1. General treatment medications, such as analgesics, antihistamines, disinfectants, hypnotics, expectorants, etc.

2. Medications used as diagnostics.

3. Medications stocked in multi-dosed vials which are comparatively inexpensive.

4. Auxiliary pharmaceutical supplies, such as diluents, solvents, and cleansing preparations.

5. Miscellaneous medications which are frequently used and inexpensive.

The tablets, vials, liquids of 16 fluidounces or less, and which comprise the above-described general purpose floor stock are distributed via a specially designed cart stocked with prepackaged quantities of drugs. Three times weekly a pharmacist visits each of the thirteen nursing units involved. The pharmacist checks the stocks on hand in the nursing unit (non-charge drugs) and if the contents of a bottle are one-third full or less, replaces it with a full one. At the same time, he reorganizes the stock, checks the emergency tray, withdraws drugs remaining from discharged patients, and inspects the general appearance of the drug locker. If drugs are to be replenished an entry is made on a prepared list for the individual nursing unit only, which is then initialed by the nurse in charge. These lists are accumulated for one month and then summarized.

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[1] Antiseptic Wash, gallon
Disinfectant Solution, 32 fluidounces
G-11 Utility Soap, gallon
Green Soap Solution, 10%, gallon
Magnesium Sulfate Solution, 50%, 32 fluidounces
Mouth Wash, ½ gallon
Wescodyne Solution, 0.48%, gallon
Benzalkonium Chloride Aqueous, 1:1000, gallon
Benzalkonium Chloride Tincture, 1:1000, 32 fluidounces

The cart used for this distribution consists of a cabinet fifty-four and one-half inches long, thirty-six and one-half inches high, forty-two inches wide at the bottom, tapering to 15 inches at the top. A vertical partition runs the length of the cart, separating the cabinet into two identical sections. There are three adjustable shelves on each side supported by brackets. The cabinet is enclosed with sliding glass panels fitted with locks. There are two metal storage cabinets beneath the shelves measuring fifty-four and one-half inches by fourteen and one-half inches by eleven inches and a pivotal pull-out drawer at the forward end of the cart measuring seventeen and one-half inches by eleven inches by twelve inches. The cabinets and drawer are fitted with locks.

The inventory of the central emergency nursing office drug locker is reviewed and carefully analyzed. The quantities to be stocked are based on usage experience. Supplies from this locker are to be dispensed by the supervisor on regular drug requisition slips. These drug slips are sent to the pharmacy the following morning and serve as a basis for replenishing locker stocks.

Procedures with Charge Drugs

As stated above, all drugs, other than free drugs, must be ordered on individual patient drug requisition slips. To speed deliveries, to reduce "emergencies," and to lessen nurses' visits to the pharmacy, a messenger service from the pharmacy was established. Inpatient drug charge requests are processed through the pharmacy by a two-hourly pick up and delivery service. The drug requisitions are placed in a bag and put into a "pick-up box" on the nurse's desk. A messenger picks up requisitions six times daily at 9:00 and 11:00 A.M. and at 1:00, 3:00, 5:00 and 7:00 P.M. Deliveries are made at 11:00 A.M. and 1:00, 3:00, 5:00, 7:00 and 8:00 P.M. This service is available seven days each week, including Sunday. Special and emergency requests by telephone are filled promptly and delivered by messenger.

Experiences with the Program

This plan went into operation January, 1958. The operation was repeatedly reviewed and evaluated for its effectiveness and efficiency. Discussions were held with nursing supervisors and nurses at the individual nursing stations. Among the observations and comments offered were the following:

1. Stocks of drugs at the nursing stations were visibily smaller in quantity. Although an inventory was not actually taken, it is the authors' impression that they have been reduced between 40 to 50 percent.

2. The drug stocks are kept in neater and more orderly fashion.

3. In most cases, individual patients' drugs are neatly stacked and identified by patient name and bed number.

4. Types and quantities of drugs on the "Standard Drug Stock List" are adequate and sufficient. Some adjustments, based on usage were made.

5. There were no difficulties encountered in ordering drugs by individual patient drug requisition slips.

6. Generally, there was little difficulty in withdrawing unused charge drugs from the nursing stations (patients being credited for unused portions).

7. The drug cart and messenger services are excellent.

8. Extended pharmacy hours have been very helpful.

9. Actual visits by nurses or others to the pharmacy have been minimized.

10. The nursing office locker has been restocked, but it is rarely used.

11. Only once or twice has it been necessary for a nursing supervisor to go to the pharmacy for an emergency drug.

12. In general, there was only praise for the new procedure by the nurses.

The advantages enumerated above principally affect the nursing units. However, the pharmacy also has experienced a number of advantages. Among these are:

1. The ability to more efficiently schedule duty rosters and functions of the pharmacy personnel.

2. Reduction of interruptions as the result of lessened "emergency" requests.

3. Permits more time for packaging operations.

4. Keep inventory records of free drug distributions, and prepare periodic reports.

5. Maintain good rapport with nursing services.

Conclusion

It is felt that the inauguration of this program was well worth the effort. It is contemplated to extend it to all nursing stations. Further, the types of drugs available on the drug cart are also to be extended. The visits to the floors by a pharmacist three times weekly alerts the pharmacy personnel to the needs and problems of the nursing units and enables them to make necessary adjustments. This is in keeping with the aims of an efficient pharmacy, viz., to supply necessary drugs in order to enable the nurse to comply promptly with the physicians' orders. In essence, the required drug must be available at the right time and at the right place when the patient is in need of it.

the human element in pharmacy management

by EDWARD F. CROUMEY

► THE CHIEF PHARMACIST OF A MODERN HOSPITAL has a dual responsibility. He must be a competent pharmacist, thoroughly versed in all of the technical aspects of pharmacy and pharmacology, as well as a business manager of one of the more important departments of the hospital.

It has been estimated that in 1957 the 7,000 hospitals in the United States spent more than $319,000,000 in purchasing pharmaceutical supplies. This represents 26 percent of the total ethical pharmaceuticals produced. The remaining 74 percent represents the purchasing of the 55,000 retail drug stores in this country.[1] Hospital pharmacy is big business. Even the small hospitals without pharmacy departments average $324.00 per bed in a year.[2]

The role of the hospital pharmacist as a professional person has appeared in the literature. His duties and responsibilities appear in the journals with every issue. Little, however, has appeared concerning his role as a business manager.

Role as Manager

The modern hospital pharmacist is more than a dispenser of drugs in the hospital organization. While dispensing is one of his more important charges, the responsibilities of the chief pharmacist, by necessity, extend beyond dispensing into other professional areas and into administration or management.

As a manager, the pharmacist devotes 90 percent of his time to dealing with people. Dr. Paul Rankin of The Ohio State University discovered that in our average working day, we spend 70 percent of our time in verbal communication. This verbal communication, according to Dr. Rankin, is broken down as follows:

30 percent of the time is spent in speaking.
45 percent of the time is spent in listening.
16 percent of the time is spent in reading.
9 percent of the time is spent in writing.

Five basic principles should enable us to increase our department's productivity and efficiency:

I. Develop personal communications.
II. Establish good inter-departmental communications.
III. Train your understudy and other people within the department.
IV. Learn to delegate responsibility.
V. Develop morale.

Personal Communications

Personal Communications consist of:

1. Understanding
2. Developing common ground
3. Tact

EDWARD F. CROUMEY is Chief Pharmacist at The Mary Fletcher Hospital, Burlington, Vermont

Presented at the Annual Convention of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, August 18, 1959 at Cincinnati, Ohio.

4. Conciliation
5. A "you" attitude
6. Giving credit
7. Getting all the facts
8. Listening

Understanding is probably the most important factor in your personal communication. By putting yourself in your employee's position, with full recognition of his status, his interests, his feelings and his welfare, you will have complete understanding of his function.

Developing a common ground is a basic tool for improving human relations. By referring to common interests, common experiences, and common understanding, we tend to bring listener and speaker closer together. The ultimate object is to make the other fellow feel that you do know and appreciate his problems. By first establishing an understanding upon which you and someone else can agree, the gulf of disagreement is narrowed and a common ground is found upon which two people can stand. The road to agreement is built on acceptance of mutual benefits and interests.

Matthew 7:12 defined *tact* very well when he said, "Whatsoever ye would that men should do to you, do ye even so to them." In other words, "Do unto others as you would have them do unto you." Should you follow these principles, you will have gone a long way toward being tactful.

Conciliation is (1) a fair hearing and an attempt to understand what the other person has said. (2) a clear, fair, and pleasant statement of the other person's point before answering him. (3) emphasizing your areas of agreement and understanding before you state your differences. (4) indicating your own position, explaining it, and supporting it fairly. (5) concluding with an open-mind attitude rather than a dogmatic insistence upon your point of view.

The *"you" attitude* rather than the "I" attitude is important in all personal relations. This means you should consider the person on the receiving end rather than only yourself.

Nothing will so improve your mutual personal relationships as *giving* an employee credit whenever you can. When your associate has been fairly praised, he will not only do a better job, but he will also serve as an excellent incentive to other workers. Beware, however, of the public reprimand, or reprimand without cause. It not only tags you as a poor department head, but also ruins your relationships with other employees.

You must have *all the facts* to make a decision. Beware of that stumbling block to clear thinking and good decisions known as "jumping" to conclusions. "Jumping" results when the decision is made without facts.

Listening sometimes becomes a most important link in the chain of personal relations. "Count ten before you speak" is another way of saying get the fact, listen, and make your decision.

Establish Good Inter-Departmental Communications

As a manager, your responsibility is to get things done through people. However sound your ideas or well reasoned your decisions, they become effective only as they are transmitted to others and achieve the desired action or reaction. Communication, therefore, is your most vital tool.

1. Learn to understand and appreciate the problems of other departments.
2. Make yourself better understood by men in other departments.
3. Communicate with superiors and subordinates on the same level.
4. Seek to clarify your ideas before communicating.
5. Examine the true purpose of each communication.
6. Consult with others, where appropriate, in planning communications.
7. Take the opportunity, when it arises, to convey something of help or value to the receiver.
8. Follow up your communications, see if you have put your message across.
9. Be a good listener. Concentrate on the meanings, unspoken words, and the undertones that may be far more significant to understanding a communication.

Training Your Understudy and Others

What are the benefits of training your understudy and other people within your department?

1. Work will go on smoothly when we are away from the job, thus relieving us of worry and giving us peace of mind.
2. We shall be relieved of some details, leaving more time for planning, for self-improvement, and for greater responsibilities.
3. It broadens us; we learn through teaching; we get the benefit of an understudy's opinion.
4. A sense of responsibility is passed down through the whole group.
5. It develops our executive ability and shows our administrator that we have the ability.
6. We learn more about the ability of people around us.
7. A stronger department is created, making our position more secure, and helping us to insure continuation of benefits.
8. Safer methods of work will evolve, protecting the patient against accidents because more trained people will be working toward that end.

Basically, what are we trying to teach our understudy? We must help our understudy to acquire all the qualities of a good leader. We must teach him to think, to be able to make up his mind and be decisive. Training is required if a person is to be able to weigh various alternatives, to be able to force his way to a conclusion, and to act on it. The understudy must be able to plan, to see problems as a whole with details in their proper perspective, and to set a course of action which will take "first things first."

The understudy must be taught to develop a strong urge to *accomplish*. He must want to get things done, learn to handle problems as they come up, dispose of them, and get on to new and still more challenging problems.

Ambition and responsibility go hand in hand. The willingness to work hard and the desire to get ahead are his main qualifications.

Tolerance, the ability to accept people pretty much as they are, is an asset in our training program.

The understudy must be able to *get along with others*. Most supervisory positions involve considerable pressures. Unless these pressures are handled constructively, the individual is likely to become overly worried and tense, to the point where his judgment and ability may be affected. Emotional maturity must be acquired and developed. Above all, one should never stop learning. A successful leader learns in many ways, but especially from experience. He must be able to analyze the reasons for success, and to guide future efforts accordingly.

What methods are available to us for training? The exact day-by-day procedure for a training program cannot be set down in schedule form. Although the exact way you go about this training will be tempered by local conditions and requirements, there are certain general techniques which experience has shown to be very helpful.[3] Two of these methods are:

1. What you think?
2. Get and interpret the facts

It is easy to say, "What do you think, Mitch?" A realization of the benefits to be derived from drawing out an understudy's opinion should make us want to use this method more and more. If, however, your understudy's ideas are not used, be sure and explain to him your reasons for not acting on his suggestion.

An understudy, to be prepared for making decisions, must be taught that judgment is only as good as the facts upon which it is based. Gathering and interpreting facts will give an understudy training in organizing an attack on a problem, in separating important and unimportant details, and in giving a complete, orderly report. The best way for learning is by doing.

Learn to Delegate Responsibility

Delegation is frequently defined as: How to get things done through people. Delegation, however, must be done slowly and in easy stages. Some of the advantages are:

1. Other people's time is saved (especially if they know more about the job than you).
2. The job is usually done better.
3. It eases your job pressures.
4. Develop assistants who are capable of acting on their own in minor emergencies.
5. Provides for assistants in your absence or for periods of uninterrupted thinking and planning.
6. It provides your personnel with the stimulus to make routine jobs more satisfying.
7. It gives your workers some group goals which make them more of a team.

Delegation of work does not mean hiring extra help, or putting extra motion into jobs. It is largely shifting some of the thinking and responsibilities from the department head's job and incorporating them into the jobs of his employees.

Brooks[4] studied carefully the habits of 96 prominent executives. They were rated on a large assortment of characteristics and work methods. The following gives a quick run-down of his results:

They Most Always, or Always	Excellent Executives %	Below Average Executives %
Had workers share in making decisions	100%	10%
Coordinated the activities of workers	100%	10%
Made full use of skills and abilities of workers	100%	10%
Saw that authority of each worker was clearly understood	83%	10%
Kept workers informed of activities in other departments	83%	10%
Kept workers informed about things affecting their work	92%	20%
Encouraged workers to exchange information	92%	20%
Knew how well workers were doing	100%	30%
Encouraged workers to express ideas and opinions	100%	30%
Selected the right person for the job	100%	30%

Delegation ranks in the top quarter of methods used by executives to accomplish more in less time with less wear and tear on the human body system.

If you are delegating to ease your immediate burden: You should delegate:[5]

1. Hangover responsibilities that originated in other jobs, situations, crises, etc., if they have no direct relation to your current function.
2. Recurring routine details.
3. Routine decision making that is time consuming to you. Only exceptional or troublesome decisions should come from you.

4. Jobs that regularly consume big chunks of your time.

5. Functions which you are least qualified to handle.

6. Details you do not like—providing you can find someone who does.

You should not delegate:

1. Any job detail which has to do with such essentially executive functions as: Setting objectives for your department. Organizing subordinates into an efficient team. Motivating and communicating with employees through planned face to face contact. Checking and analyzing results as guides to future plans. Developing subordinates in job skills and routine decision making.

2. Duplicating responsibility in which the delegate is permitted to feel he has been given a miniature of the chief's position. As a safeguard, set a definite goal with clearly defined boundaries, such as: "Run down the reasons for this criticism and let me know what you think we should do about it."

3. Disciplinary power. Make certain the delegate understands he is expected not to use threats or discipline to reach his objective.

4. Decision-making which involves the objectives of the hospital or of your own particular department.

5. Decision-making which involves inter-hospital or inter-departmental relations, future plans or personnel.

6. Complete responsibility. Delegating a job does not mean "dumping" it.

To develop employees you should delegate:

1. Tasks that lead to skills or mold attitudes of the individual.

2. Tasks that will provide more variety in the employee's job.

3. Jobs involving enough challenge to stimulate an employee, but avoid tasks that may hobble or frustrate him.

4. A sequence of jobs on which you feel sure the employee will do well. This helps him develop by providing an increasingly challenging task each time he has mastered one of less complexity.

Andrew Carnegie made no secret of his use of delegating to get things done through others and to ease the job pressure on himself. He had frequently stated, "It marks a big step in a man's development when he comes to realize that other men can be called in to help him do a better job than he can do alone."

Develop Morale

All of the previous suggestions lead into the net result, which is good morale. Just what is morale?

Morale in a business or hospital family is an attitude of emotional readiness which enables the worker to turn out more and better work without increase in fatigue, which enables him to enter enthusiastically into the activities of the department; and which makes him less susceptible to outside influences.

Some of the more significant of these conditions for which the chief pharmacist is responsible are summarized:

1. There should be friendly, skillful, and adequate introductions to the job. In the first few days, more can be done to make or mar the new employee's future than in weeks at any other time.

2. Employees should know that their efforts are appreciated. Take every honest opportunity to commend the worker. Favorable comments should not only be made of his work in the department, but also on his outside activities.

3. Feelings should be appreciated. Treat the employees like human beings. They, too, are men of pride and respect.

4. All should be treated fairly and impartially.

5. Corrections should be made with fairness and consideration. Get all the facts, choose a private place, give him a chance to give his side of the story, fit the method of correction to the individual, and close the meeting on a pleasant note.

At the Mary Fletcher Hospital we try to practice what we preach. Two years ago, realizing that the management of employees was becoming an important factor in our daily work, the hospital retained a Professor of Economics at the University of Vermont to conduct a class in supervision. He conducted weekly classes, composed of department heads and nursing supervisors.

At these meetings the many aspects of efficient handling of employees were studied. Small groups presented many cases of actual problems within the hospital. These were then discussed and solutions offered.

At the end of the lecture series each student wrote out a case study. One study concerned the many steps it took a prescription to travel from the Outpatient Clinic to the Pharmacy and return. It was determined that prescriptions were being handled by nine different employees. As a result of that study the system was streamlined, with an increase in efficiency in all departments.

Prior to this lecture series the department had occasional difficulty with nursing supervisors seeking out the Medical Director whenever some problem concerning Pharmacy occurred. This not only caused "ill feeling" between Pharmacy and Nursing but occupied too much of the Director's time in solving petty problems.

Now when either department has a problem the department heads get together and solve it between themselves. Each department head realizes the other's problem and steps are taken to help each other, not fight each other.

In the fall of 1958 this supervisory course was extended to include the head nurses and nursing students. A series of two-hour lectures were initiated. The senior nursing students have the opportunity to work with the head nurse in actual ward problems. Techniques in handling dietary, housekeeping and other personnel working on the nursing floors are discussed.

As a result of this course, "The Art of Supervision," there has been less conflict among the various departments. Each supervisor now has some idea how to handle work situations between themselves and other employees.

While maybe not all of our conflicts are resolved exactly as we want them, an intelligent compromise can be made. We are now a team and not a mob.

Dr. J. Gilbert Turner* in a speech presented before the Vermont Hospital Association in Burlington, Vt., summarized very well the responsibilities of the chief pharmacist as a manager, when he said:

"1. Are you proud of your position and of your hospital? You must believe in your job to do your best.

2. Is your department organized efficiently? You cannot get maximum performance without a plan.

3. Are hospital policies made known to you? There must be a blue print of action.

4. Is there good liaison between you and your director? You should not burden him with trifles; nor should you be left to your own. Yours is the initiative.

5. Do you have an approved budget both for salaries and equipment? Do you insist upon preventive maintenance as well as regular maintenance? Do you get monthly budget reports promptly"? These are important tools in efficient management.

6. Do you have a deputy trained who can carry on adequately while you are away for short or long periods?

7. Do you have established procedures whereby you or your deputy can be available for emergencies after hours?

8. How much do you know about the functions of other departments?

9. Do you sometimes take to task employees of another department when you well know you wouldn't tolerate for a moment another department head doing the same to your employees?

10. What techniques do you use to keep up to date with developments? Conferences within the hospital? Meetings in your community with those of interests similar to your own? Membership in professional organizations? Attendance at hospital meetings? Are you a regular reader of hospital literature? If extension courses are available in your own or allied fields, do you take advantage of them?

11. How are the personnel policies of your department? How high is your turnover? If employment is terminated, is the employee satisfied that his treatment was fair?

12. Do you keep your administrator informed?

13. Can you take orders as well as give them?

14. Are you sure that there is absolutely no waste in your department—no waste of effort—no waste of time—no waste of material or supplies?

15. Do you welcome changes in procedures when such changes seem reasonable?

16. Are you continually seeking ways and means to improve your departmental efficiency?

17. Do you recognize the importance of a study of departmental operations by selected outside experts?"

Conclusion

1. The pharmacist of today is no longer simply a technical person; he now has a dual responsibility as a professional and as an administrative or management specialist.

2. He is not the push-button type of executive but a dynamic, forceful, individual who believes in what he is doing and knows how to do it with the tools that are available.

3. The Department of Pharmacy under proper supervision and good management can be an excellent example of efficiency as an important teammate with the nursing and medical staffs, all working together for increasingly better patient care.

Bibliography

1. Mannino, A.: Hospital Pharmacist—Business Manager Extraordinary, Talk presented at the Pharmacy Section of the American Association for the Advancement of Science, Indianapolis, Ind., December, 1957.

2. Berman, A.: Pharmacy Service in Smaller Hospitals, Part I, *Am. Profess. Pharm. 23*:1066 (Dec.) 1957; Part II, *ibid. 24*:50 (Jan.) 1958.

3. Carnegie, Illinois Steel Company Film: "How to Prepare for the Future."

4. *Personnel 32*:210.

5. Laird: *Management Methods 12*:50 (Aug.) 1957.

Supplemental Reading

Small Business Administration Bulletins.

Surveying and Controlling Executive Time, *Management Aids for Small Manufacturers,* September, 1956.

Job Evaluation in Small Industry, *Ibid.* (May) 1958.

How to Analyze Your Own Business, *Ibid.* (Mar.) 1958.

Pricing Arithmetic for Small Business Managers, *Ibid.* (Feb.) 1959.

Executive Development in Small Business, *Small Business Administration* Series Number 12.

Better Communications in Small Business, *Ibid.,* Number 7.

Applied *Creative Thinking, Office Management Conferences 1956–1957* The Goodyear Training Division, Goodyear Tire and Rubber Company.

You and I in Communication, *Ibid.*

Personnel Practice, *Ibid.*

Man to Man On the Job, General Motors Corporation.

Staff Development, Training Manual Number 6, Department of Health, Education and Welfare, Washington, D.C.

*J. Gilbert Turner, M.D., C.M., M.Sc., F.A.C.H.A., Executive Director, Royal Victoria Hospital, Montreal.

THE FUTURE OF HOSPITAL PHARMACY EDUCATION IN GEORGIA

by CHARLES W. HARTMAN

► THE FIFTH LARGEST INDUSTRY IN THE UNITED States is hospitals. In Georgia, in 1956, hospital services amounted to 51.3 million dollars. About 10 percent or 5 million dollars of this was spent on pharmaceuticals.

CHARLES W. HARTMAN is Associate Professor of Pharmacy, School of Pharmacy, University of Georgia, Athens, Georgia.

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The purpose of the present paper is to show that educators in pharmacy must awaken to the vast expansion program of hospitals that is taking place.

Twenty percent more Georgians are taking advantage of hospital services now than in 1950. With

TABLE 1. VOLUME OF GENERAL HOSPITAL SERVICES, GEORGIA, 1950 - 1956*

YEAR	NO. OF PATIENTS ADMITTED	NO. OF PATIENT DAYS	AVERAGE LENGTH OF STAY PER PATIENT (DAYS)	ADMISSIONS PER 100 POPULATION	HOSPITAL COST PER PATIENT DAY (DOLLARS)	ESTIMATED TOTAL EXPENDITURE FOR HOSPITAL SERVICE (MILLIONS OF DOLLARS)
1956	427,300	2,422,280	5.67	11.8	21.18	51.3
1955	400,000	2,232,000	5.60	11.1	20.12	44.8
1954	398,000	2,212,000	5.50	11.1	19.44	43.1
1953	394,571	2,095,756	5.31	11.3	17.97	35.7
1952	362,234	2,074,089	5.73	10.7	17.82	33.6
1951	338,463	1,947,660	5.75	9.9	14.85	31.5
1950	316,390	1,875,130	6.00	9.3	12.95	24.2

*SOURCE: Division of Hospital Services, Georgia Department of Public Health (Data is for calendar year)

Table 2. Use of Hospital Pharmacists by Hospitals - National Average*

Hospital Size, Beds	Percent That Have A Pharmacy
Under 25	20.2
25 - 49	30.7
50 - 99	51.6
100 - 199	85.8
200 - 299	97.7
300 - 499	99.6
Over 500	100.0

Hospitals, Journal of the American Hospital Association Table No. 16, Pages 398-99, August 1, 1957.

the increase in population added to this, there has been an increase of approximately 35 percent in admissions to hospitals since 1950. (See Table 1.)

Table 2 shows the national average of the use of pharmacists by hospitals. This is, of course, only an average and it must be kept in mind that some hospitals are providing complete protection of their patients with regard to pharmaceutical services whereas others are wholly negligent in this respect. However, in an effort to show the position of hospital pharmacy in Georgia, the national average has been used as a comparison. The method used in calculating the number of pharmacists needed to meet the national average is given in Table 3.

The method of determining the minimum number of pharmacists needed to adequately staff hospitals in Georgia is given in Table 4. This would give, of course, only adequate pharmaceutical service and would not allow for complete 24 hour protection by pharmacists, drug cabinet inspections on wards, safety instruction on pharmaceuticals for other personnel, pharmacy and therapeutics committee meetings, and many other protective measures needed to properly control pharmaceutical services.

Table 3. Method Used to Calculate Pharmacists Needed in Georgia Hospitals to Meet Level of National Average

Under 25 (Not Calculated)	
No. of Hospitals 25 to 40 Bed Capacity X 25%	
No. of Hospitals 40 to 49 Bed Capacity X 30%	
No. of Hospitals 50 to 99 Bed Capacity X 52%	
No. of Hospitals 100 to 199 Bed Capacity	$\frac{\text{x 86\% x Beds}}{100}$
No. of Hospitals 200 to 299 Bed Capacity	$\frac{\text{x 98\% x Beds}}{100}$
No. of Hospitals 300 to 499 Bed Capacity	$\frac{\text{x 100\% x Beds}}{100}$
No. of Hospitals Over 500 Bed Capacity	$\frac{\text{x 100\% x Beds}}{100}$
Mental Hospitals:	Total Beds ÷ 2000
Chronic Hospitals:	Total Beds ÷ 1000
Nursing Homes:	Total Beds ÷ 1000
Tuberculosis Hospitals:	Total Beds ÷ 650

Table 5 is a complete analysis of the need for hospital pharmacists in Georgia.

Table 6 is a summary of the needs of hospitals in Georgia for hospital pharmacists. These pharmacists cannot come from the normal supply of pharmacists by the schools at present. With the increase in prescription volume in retail pharmacies the need for pharmacists in this area will become even greater. Also, there are still approximately 50 percent of the retail pharmacies in Georgia operating with only one pharmacist.

The supply of hospital pharmacists must and can come from the schools. This is evidenced by the success at the University of Georgia School of Pharmacy of a one quarter elective course in hospital pharmacy. This course was initiated in 1953 and since that time eleven people who have taken the course are now employed in hospital pharmacies in Georgia. These eleven people represent about 13 percent of the hospital pharmacists in Georgia. If this one three hour elective course can do this much in five years, think of the influence a specialized program in hospital pharmacy could have on the future of hospital pharmacy in Georgia. In addition to the course in hospital pharmacy, every senior pharmacy student serves a 30 hour internship in a hospital pharmacy. This not only exposes the student to the needs and functions of a hospital pharmacy, but this experience makes him better prepared to work as a part of the public health team regardless of the field of pharmacy he chooses for his future. A program of hospital pharmacy study outlined to meet the needs of small hospitals would be a public health service and prove economical to the state of Georgia.

The following is a suggested type of program that would best fit the needs of Georgia hospitals.

1. Pharmacy School - Hospital Intern Programs.
2. Specialized courses in hospital pharmacy.
3. Courses to qualify pharmacists for purchasing agent's position.
4. Courses to qualify pharmacists for assistant administrator's position (or administrator in small hospitals).

Table 4. Number of Pharmacists Needed According to Bed Capacity of Hospital

Bed Capacity	Pharmacists Needed
Under 50	1
100	2
200	3
300	4
400	5½
500	6½
600	8
700	9
800	11
900	12
1000	13

TABLE 5. ANALYSIS OF NEED FOR HOSPITAL PHARMACISTS IN GEORGIA

CITY OR HOSPITAL	PRESENT BED CAPACITY	TOTAL BED CAPACITY PLANNED	PHARMACISTS NEEDED TO MEET LEVEL OF NATIONAL AVERAGE	PHARMACISTS NEEDED FOR ADEQUATE 24 HOUR PROTECTION OF PUBEIC HEALTH
Decatur	0	392	3.92	6.0
Buford	21	40	.12	1.0
South Fulton	0	287	2.81	4.0
West Fulton	0	100	.86	2.0
Rome	222	344	3.40	1.0
West Point	0	40	.12	1.0
Warm Springs	32	42	.13	1.0
Camilla	50	50	.15	1.0
Dalton	75	170	1.46	3.0
North Dekalb	0	250	2.46	3.5
Lagrange	199	253	2.48	3.5
Albany	243	283	2.78	4.0
Calhoun	40	66	.34	1.0
Chattsworth	32	42	.13	1.0
Newnan	66	178	1.43	6.0
Carrollton	42	52	.27	1.0
Ft. Oglethorp	110	267	2.62	3.5
Atlanta	2,785	2,785	27.85	37.0
Duluth	27	40	.12	1.0
Lawrenceville	35	45	.14	1.0
Macon	592	642	6.42	8.5
Royston	35	43	.13	1.0
Milledgeville	75	104	.93	2.0
Jesup	69	87	.44	2.0
Elberton	48	75	.39	1.5
Eastman	0	40	.12	1.0
McRae	31	42	.13	1.0
Douglas	60	81	.42	2.0
Sandersville	0	71	.36	1.5
Greensboro	65	65	.33	1.0
Louisville	38	52	.27	1.0
Hawkinsville	60	73	.38	1.5
Cuthbert	50	61	.31	1.0
Augusta	610	742	7.42	10.0
Thomson	29	40	.12	1.0
Savannah	787	822	8.22	11.0
Brunswick	127	192	1.65	3.0
St. Marys	0	40	.12	1.0
Statesboro	100	100	.86	2.0
Swainsboro	68	68	.35	1.0
Waycross	100	139	1.19	2.5
Waynesboro	. 39	50	.26	1.0
Millen	40	50	.26	1.0
Sylvania	34	45	.14	1.0
Dublin	60	89	.46	2.0
Vidalia	28	49	.14	1.0
Columbus	380	565	5.65	7.5
Marietta	251	340	3.40	4.5
Douglasville	35	45	.14	1.0
Griffin	96	230	2.25	3.0
Gainesville	172	232	2.27	3.0
Athens	261	331	3.31	3.5
Moultrie	129	165	1.42	3.0
Americus	125	143	1.23	2.5
Valdosta	100	150	1.30	2.5
Thomaston	93	109	.93	2.0
Canton	50	90	.47	2.0
Jasper	0	40	.12	1.0
Tifton	65	65	.34	1.0
Bainbridge	30	105	.93	2.0
Cedartown	52	82	.43	2.0
Covington	34	50	.26	1.0
Cordele	50	50	.26	1.0
Montezuma	80	80	.42	2.0
Perry	0	60	.31	1.0
Fitzgerald	0	41	.12	1.0
Toccoa	49	118	1.01	2.0
Demorest	43	43	.13	1.0
Commerce	0	48	.14	1.0
Monroe	45	45	.15	1.0
Winder	40	40	.12	1.0

5. Courses to qualify pharmacists for laboratory supervisor's position.
6. General courses in public health management.

The need is here now. We cannot fail to recognize the dangers involved in pharmaceutical services in Georgia hospitals that are not properly staffed.

How big should a hospital be to need the service of a pharmacist? This is defined very clearly by Georgia Law, Hospital Regulations Act, Act 623, Georgia Law 1946, Part II, Section VI.

"77. When a dispensing and manufacturing pharmacy is maintained, only a registered pharmacist licensed to practice in the state of Georgia may fill prescriptions and compound preparations for the hospital."

You and I know that any hospital must do some dispensing and some manufacturing in order to provide proper pharmaceutical services for patients.

Let us hope that those responsible for guidance in the protection of public health in Georgia will accept and meet the challenge.

TABLE 6. PHARMACISTS NEEDED TO STAFF GENERAL HOSPITALS PLANNED AND SPECIAL HOSPITALS PLANNED OR NEEDED IN GEORGIA IN 1957

	TOTAL BEDS NEEDED AND PLANNED	PHARMACISTS NEEDED TO MEET LEVEL OF NATIONAL STANDARDS	PHARMACISTS NEEDED FOR ADEQUATE 24 HOUR PROTECTION OF PUBLIC HEALTH
Chronic Hospitals	6,804	6.80	10
Nursing Homes	9,354	9.35	10
Mental Hospitals	18,175	9.08	18
Tuberculosis Hospitals	2,000	3.00	6
General Hospitals	16,358	112.42	198
Total Pharmacists Needed all Hospitals		140.65	242
Pharmacists Now Employed		79.00	79
Additional Pharmacists Needed For Hospitals over 40 Beds		61.65	163
64 Hospitals Less Than 40 Beds But More Than 25		16.00	64
Actual Additional Needs For Pharmacists		77.65	227

Therapeutic Trends

edited by WILLIAM JOHNSON

Compound 1757 I.S.—A Convulsant Drug

An investigation of the convulsant properties of 5-7-diphenyl-1-3-diazodamantan-6-ol (1757 I.S.) is reported in *J. Pharmacol. Exp. Ther. 126*:41 (May) 1959. 1757 I.S., a new synthetic convulsant agent, showed remarkable similarity in convulsant activity to strychnine. These two substances show no similarity in chemical structure, yet it is suggested that these compounds have a common mechanism of action, which is based on interference with central mechanism of integration. One group of investigators suggests that strychnine has a specific action based upon its blockage of the inhibitory systems present at various levels of the C.N.S. Mice, rats, and rabbits were used as test animals and the effects of anticonvulsants and depressants, effects on the cardiovascular and respiratory systems, and studies on toxicities and electroencephalographs of the actions of 1757 I.S., strychnine, pentylenetetrazol, picrotoxin and nikethamide were compared for the evaluation of 1757 I.S.

DALE R. HYDER

Ethoxzolamide—A New Anticonvulsant

The anticonvulsant effect of ethoxzolamide was studied in a small group of patients by Solomon and Hirano. Their results were reported in *Neurology 9*:167 (Mar.) 1959. Twenty-five patients who had been under poor control were used in this study. These patients had previously tried several other available anticonvulsants. Ethoxzolamide brought under excellent control most patients with grand mal and petit mal seizures. The effect the drug had on patients with psychomotor seizures was evident but less pronounced. Side effects were minimal in this group and caused the discontinuance of the drug in 2 of 25 people. The most common side effect was dizziness. The anticonvulsant properties seemed to be in direct proportion to the degree of carbonic anhydrase inhibition effect the drug has in the brain. Because of the high potency as a carbonic anhydrase inhibitor, ethoxzolamide appears to be a significant addition to the field of anticonvulsants. Ethoxzolamide was supplied for this study as Cardrase by the Upjohn Company.

RICHARD H. HARRISON

Use of Intravenous Priscoline in the Treatment of Subdeltoid Bursitis

The treatment of acute subdeltoid bursitis has consisted of many and varied physical and medical methods. Frankel and Strider suggest the use of Priscoline in *Amer. Pract. Dig. Treat. 10*:830 (May) 1959. One hundred and fifty patients were given one to three intravenous injections of 25 mg. of Priscoline hydrochloride at daily intervals for a period of one to three days. The range of motion in the affected extremity was measured previous to and following the injection, the improvement or lack of improvement being noted. Seventy-one cases were graded as excellent in response, sixty-eight as good, and eleven as failures. It is believed that the pain is caused by an autonomic disturbance which maintains a state of irritability at the terminal end of the pain receptors. Priscoline, having a sympatholytic action, is thought to exert its action by producing a chemical sympatholytic block in the efferent elements of the circuit, especially in the sympathetic fibers.

KENNETH W. HUCKENDUBLER

New Usage of Podophyllin

A case of papillomatosis of the bladder has been presented which to date has been treated successfully with bladder instillations of podophyllin. The treatment consisted of four appointments using increasing percentages of 1, 4, 8, and 12 percent podophyllin in three ounces of mineral oil for a gradual lengthening of time. Before podophyllin was used, cystectomy was usually required. Podophyllin treatment has no value in infiltrating bladder tumors. However, if patients with generalized papillomatosis of the bladder can be saved cystectomy by this method, then it should be tried. This report was given by Edward Richardson in *J. Urol. 82*:234 (Aug.) 1959.

SYLVIA SCHMIDT

Timely Drugs

Actifed

COMPOSITION: Triprolidine (Actidil) hydrochloride and pseudoephrine (Sudafed) hydrochloride.

INDICATIONS: Prophylaxis and treatment of symptoms associated with common cold, and allergic conditions including hay fever, pollenosis, allergic asthma, etc. An orally administered nasal decongestant and bronchodilator with antihistaminic action.

DOSAGE: Adults, 1 tablet or 2 teaspoonfuls of the syrup 3 times a day; children 4 months to 6 years, ½ tablet or 1 teaspoonful 3 times daily; infants through 3 months of age, ½ teaspoonful syrup 3 times daily.

PREPARATIONS: Tablets containing triprolidine hydrochloride 2.5 mg. and pseudoephedrine hydrochloride 60 mg.; syrup containing in each 5 ml., triprolidine hydrochloride 1.25 mg. and pseudoephrine hydrochloride 30 mg.

PACKAGING: Bottles of 100 tablets and bottles of 1 pint of syrup.

SUPPLIER: Burroughs Wellcome & Co.

Ademol

GENERIC AND CHEMICAL NAMES: Flumethiazide. 6-(Trifluoromethyl)-1,2,4-benzothiadiazine-7-sulfonamide-1,1-dioxide.

INDICATIONS: Oral, nonmercurial diuretic, equivalent to chlorothiazide, its chloro homologue. Indicated in all patients manifesting edema from whatever cause, in patients with abnormal fluid retention with or without clinically apparent edema, whenever a low-salt diet is necessary, and in the management of hypertension.

SIDE EFFECTS AND CONTRAINDICATIONS: A few cases of mild pruritus and minor gastrointestinal disturbances; contraindicated in cases of complete renal shutdown.

DOSAGE: In edema, 0.5 to 2 Gm. daily in divided doses, preferably in morning and early afternoon to avoid nocturnal diuresis; maintenance, 0.25 to 1 Gm. daily in divided doses. In hypertension, initially 0.5 to 2 Gm. daily in divided doses; maintenance, 0.5 to 1.5 Gm. daily in divided dosage.

PREPARATIONS: Tablets containing 0.5 Gm.

PACKAGING: Bottles of 60 tablets.

SUPPLIER: E. R. Squibb & Sons.

Calurin

CHEMICAL NAME: Calcium aspirin.

INDICATIONS: Highly soluble form of aspirin for use when long-term therapy is indicated; sodium-free; high solubility forestalls gastric irritation or damage.

DOSAGE: For relief of pain and fever, usual adult dose is 1 to 3 tablets every 4 hours; in arthritic states, 2 or 3 tablets 3 or 4 times daily; in rheumatic fever, 3 to 5 tablets 4 or 5 times daily. Children 6 to 12, 1 tablet; children 3 to 6, one-half to one tablet, every 4 hours.

PREPARATIONS: Tablets containing the equivalent of 0.3 Gm. acetylsalicylic acid.

PACKAGING: Bottles of 100 tablets.

SUPPLIER: Smith-Dorsey.

CR-Test

INDICATIONS: Rapid slide test for determination and quantitation of C-reactive protein. Combines C-reactive protein antibody with polystyrene latex particles, producing a reagent which gives visible test results in one to two minutes on a glass slide.

PROCEDURE: For screening procedure, a drop of the patient's serum is mixed with the reagent. If C-reactive protein is present, flocculation will occur. In quantitative test, serial dilutions of serum specimen are prepared in glycine-saline buffer diluent; one drop of each serum dilution is mixed with reagent; highest serum dilution showing visible flocculation is taken as the C-reactive protein titer of the specimen.

PACKAGING: Kits containing Latex-Anti-C-Reactive Protein Reagent, Glycine-Saline Buffer Diluent, capillary pipettes and two divided glass slides. Each kit is sufficient for 60 tests.

SUPPLIER: Hyland Laboratories.

Decabamate

COMPOSITION: Dexamethasone and meprobamate.

INDICATIONS: For symptomatic therapy in allergic and inflammatory disorders responsive to treatment, especially when accompanied by excessive anxiety and tension or, in the case of rheumatism and arthritis, by fibrositis and muscle spasm.

SIDE EFFECTS AND CONTRAINDICATIONS: Patients should be observed for signs of corticosteroid toxicity plus side effects which may accompany therapy with meprobamate.

DOSAGE: Depends upon nature and severity of condition being treated; recommended dosage is one or two tablets 3 or 4 times daily.

PREPARATIONS: Tablets containing dexamethasone 0.25 mg. and meprobamate 200 mg.

PACKAGING: Bottles of 100 tablets.

SUPPLIER: Merck Sharp & Dohme.

Dechotyl

COMPOSITION: Dehydrocholic acid (Decholin), desoxycholic acid, and dioctyl sodium sulfosuccinate.

INDICATIONS: To correct constipation physiologically, especially that associated with the irritable bowel syndrome; increases flow of bile, provides gentle stimulation of peristalsis, and enhances penetration of fluids into the feces.

DOSAGE: Two tablets at bedtime. Some individuals may require initially 1 to 2 tablets 3 or 4 times daily.
PREPARATIONS: Tablets containing dehydrocholic acid 200 mg., desoxycholic acid 50 mg., and dioctyl sodium sulfosuccinate 50 mg.
PACKAGING: Bottles of 100 Trablets (trapezoid-shaped tablets).
SUPPLIER: Ames Co.

Emprazil

COMPOSITION: Pseudoephrine hydrochloride (Sudafed), chlorcyclizine hydrochloride (Perazil), aspirin, acetophenetidin, and caffeine.
INDICATIONS: Nasal decongestant, analgesic, antihistaminic, and antipyretic.
SIDE EFFECTS AND CONTRAINDICATIONS: Use with caution in hypertension.
DOSAGE: Adults, one or two tablets 3 times daily; children 6 to 12 years of age, one tablet 3 times daily.
PREPARATIONS: Tablets, orange and yellow layered, containing pseudoephedrine hydrochloride 20 mg., chlorcyclizine hydrochloride 15 mg., aspirin 200 mg., acetophenetidin 150 mg., and caffeine 30 mg.
PACKAGING: Bottles of 100 and 1,000 tablets.
SUPPLIER: Burroughs Wellcome & Co.

Hispril

GENERIC NAME: Diphenylpyraline.
INDICATIONS: Antihistamine, for relief of allergic manifestations, hay fever, allergic rhinitis, upper respiratory infections, urticaria, angioneurotic edema, etc.
SIDE EFFECTS AND CONTRAINDICATIONS: Usually mild or moderate, include drowsiness.
DOSAGE: Adults, one 2 mg. tablet 3 or 4 times daily or one 5 mg. Spansule every 12 hours; children 6 to 12, usually the same as adult dosage; younger children, under 6, 1 mg. once or twice daily.
PREPARATIONS: Sustained release capsules (Spansules) containing 5 mg. and tablets, scored, containing 2 mg.
PACKAGING: Bottles of 30 Spansules and bottles of 50 tablets.
SUPPLIER: Smith, Kline & French Laboratories.

Niamid

GENERIC AND CHEMICAL NAMES: Nialamide; N-[2-(benzylcarbamyl)ethylamino]isonicotinamide.
INDICATIONS: Antidepressant used in involutional melancholia, postpartum depression, manic depressive disease in depressive stage, schizophrenic reaction with depressive symptomatology, etc.
SIDE EFFECTS AND CONTRAINDICATIONS: Include nervousness or restlessness and insomnia, headaches, weakness, lethargy, vertigo, dryness of the mouth, and increased perspiration; care should be used when administering in conjunction with chlorothiazide compounds since hypotensive effects have been observed in some patients receiving combined therapy.
DOSAGE: Initially, 75 mg. daily, in one or divided doses; maintenance dose may be as low as 12.5 mg. daily.
PREPARATIONS: Tablets containing 25 mg. and 100 mg. nialamide.
PACKAGING: Bottles of 100 tablets.
SUPPLIER: Pfizer Laboratories.

Parafon with Codeine

COMPOSITION: Chlorzoxazone (Paraflex), acetaminophen (Tylenol), and codeine phosphate.
INDICATIONS: Skeletal muscle relaxant plus potent analgesic action necessary to relieve severely painful musculoskeletal disorders; useful in low back disorders such as lumbago, bursitis, tendinitis, etc.
SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally, mild nausea, drowsiness or dizziness.
DOSAGE: One to two tablets 3 or 4 times daily.
PREPARATIONS: Tablets, scored, containing chlorzoxazone 125 mg., acetaminophen 300 mg., and codeine phosphate 15 mg.
PACKAGING: Bottles of 24 tablets.
SUPPLIER: McNeil Laboratories, Inc.

Quadrigen

COMPOSITION: Diphtheria and tetanus toxoids and poliomyelitis and pertussis vaccines.
INDICATIONS: For simultaneous immunization of young children against diphtheria, tetanus, pertussis, and poliomyelitis.
SIDE EFFECTS AND CONTRAINDICATIONS: Local and systemic reactions are usually mild, usually no greater than following use of the trivalent vaccine; although residual antibiotics, e.g., streptomycin and penicillin, in the adsorbed product are not demonstrable by standard laboratory tests, consideration should be given to possibility of allergic reactions in individuals sensitive to these antibiotics.
DOSAGE: Infants between 3 and 6 months, 4 equal doses of 0.5 ml. each, given at monthly intervals; infants 6 months or older, 1.5 ml. divided into 3 equal doses of 0.5 ml. each administered intramuscularly at intervals of from 4 to 6 weeks, followed by an additional injection of 0.5 ml. after 6 to 12 months. CAUTION: Not recommended for immunizing persons over 6 years of age.
PREPARATIONS: Diphtheria and tetanus toxoids and poliomyelitis and pertussis vaccines, aluminum phosphate adsorbed.
PACKAGING: Vials of 4.5 ml.
SUPPLIER: Parke, Davis & Co.

Vasodilan

GENERIC AND CHEMICAL NAMES: Isoxsuprine hydrochloride. 1-(p-Hydroxyphenyl)-2-(1'-methyl -2'- phenoxyethylamino) propanol-1 hydrochloride.
INDICATIONS: In peripheral vascular disease for the symptomatic relief of intermittent claudication, coldness or numbness of extremities, leg pain, and trophic ulcers associated with arteriosclerosis obliterans, etc.; in cerebral impairment wholly or partially due to deficient circulation resulting from arteriosclerosis or hypertension. The use of Vasodilan as a uterine relaxant was summarized on page 409 of the August issue of this JOURNAL.
SIDE EFFECTS AND CONTRAINDICATIONS: Occasionally, palpitation and dizziness; intramuscular administration is not recommended in presence of hypotension or tachycardia; intravenous administration is *not* recommended.
DOSAGE: Orally, 10 to 20 mg. three or four times daily; intramuscularly, 5 to 10 mg. two or three times daily.
PREPARATIONS: Injections containing 5 mg. per ml. and tablets of 10 mg.
PACKAGING: Injection, ampuls of 2 ml. in boxes of 6 ampuls; tablets, bottles of 100.
SUPPLIER: Mead Johnson & Co.

THE LAW

of hospital pharmacy

edited by GEORGE F. ARCHAMBAULT

This month, this column presents for the first time, a run-down of the Pharmacy Laws of one state - Alabama. We hope in future numbers of the JOURNAL *to give to you a summary of the laws affecting hospital pharmacy practice in all states of the Union.*

The Editor of the column is most pleased to have as the guest editor this month, a pharmacist-hospital administrator — a Blue Cross-Blue Shield executive who knows well the pharmacy code of his state.

Joe Vance is well known to most of you, I'm sure. He currently serves as Assistant Executive Director for Blue Cross-Blue Shield of Alabama; was formerly a hospital pharmacist and until fairly recently a hospital administrator. Many of you know him for his monthly Pharmacy Column in Southern Hospitals.

HOSPITAL PHARMACY AND ALABAMA LAW

► HOSPITAL PHARMACIES, REGISTERED VOLUNTARILY with the Alabama State Board of Pharmacy, received this year a brand new special Hospital Pharmacy Permit.

Hardly anyone was totally satisfied with the language of the permit.

Hospital Administrator D. O. McClusky, Jr., who is a pharmacist, said: "Why, under it, I can't even sell to my own employees." He was referring to the language which says: " . . . Hospital Pharmacy is *limited* to rendering adequate pharmaceutical service to patients *residing* in the . . . hospital . . . subject to House Rules adopted by the pharmacist in charge in cooperation with the hospital administrator and approved by the Alabama State Board of Pharmacy." In reply to the McClusky comment, Alabama Pharmacy Board Secretary E. W. Gibbs said: "This does not restrict selling to employees nor prohibit outpatient service, if it is spelled out in the House Rules and falls short of doing a general outside prescription business."

Hospital pharmacist Ed Whiddon, President of the Society of Alabama Hospital Pharmacists, said: "It isn't what we would want, exactly, but it represents a beginning." Gibbs replies that adoption of House Rules which "fit into the general pattern of the permit" will clarify the questions not answered specifically by the permit.

Background

Except for an occasional attempt to logroll a local bill in order to license a political friend of a state legislator, Alabama's pharmacy laws have remained stable and largely under enforcement by the State Board of Pharmacy. The basic law is contained in the Alabama Code of 1940, Chapter 12, Title 46.

In 1947, a control measure for barbiturates was approved and placed under the enforcement authority of the Pharmacy Board.

In 1949, the State enacted a hospital licensing law (Act 530). Pharmacists cooperated with the Hospital Association in backing this law. While the hospital licensing responsibility is vested in the State Board of Health, a strong Licensure Advisory Committee supervises the entire program. Pharmacy has a representative on this Committee. The rules and regulations, both for hospitals and nursing homes, are reviewed, recommended and enforced by the Board of Health with the cooperation of this Advisory Committee. The Board of Health has consulted with the Board of Pharmacy each time a question concerning regulation of the practice of pharmacy in the hospital or nursing home has arisen.

The New Hospital Pharmacy Permit

Until 1959, hospital pharmacies which *voluntarily* registered with the State Board of Pharmacy were issued a regular retail pharmacy license and thus were subject to annual survey by an inspector from the Pharmacy Board. Those hospitals which did not choose to register their pharmacies were not routinely subject to inspection. The Pharmacy Board inspector based his annual survey of hospital pharmacies on the pharmacy law and its regulations, even though there was nothing specific in the existing law concerning hospital pharmacy.

At the instance of D. O. McClusky, Jr., a pioneer Alabama hospital pharmacist, the Board, in about 1943, agreed to issue the retail license to hospital pharmacies. This retail license entitled hospital pharmacies to give credit for the one-year practical experience period prior to final registration. In substance they had all the prerogatives of a retail pharmacy, including the privilege of employment and training of the pharmacy student.

Pharmacy Licensing Regulations of the Board of Health

A Board of Health surveyor is responsible for review of the hospital pharmacy practice under the Hospital and Nursing Home Licensing Law. The regulation says, in part: "In hospitals where patients are treated by surgery and medicines, and there is need for compounding prescriptions in the hospital, there shall be installed a hospital pharmacy under the immediate and direct supervision of a duly licensed Alabama pharmacist, properly registered with the Board of Pharmacy.

"Drugs shall not be administered to individual patients nor to anyone within or without institution, unless ordered by a physician duly licensed to prescribe drugs, and such order shall be in writing over the physician's signature."

In practice the Board of Pharmacy, the Board of Health and Alabama hospital administrators have taken this regulation to mean it is not necessary to have a registered pharmacist on duty, *unless* there is regularly a *need for compounding* prescriptions.

On the other hand, Section 234 of the Pharmacy Law of the Alabama Code 1940 says in part: "It shall be unlawful for any person, firm, corporation, or co-partnership . . . to conduct a place of business . . . in which drugs, medicines, or poisons are retailed, compounded and dispensed . . . without placing in active personal charge and on duty at all times during business hours except for temporary abscences as defined and described by the Board of Pharmacy . . . a pharmacist duly registered, etc . . . "

The Pharmacy Board has apparently interpreted this part of the Code to mean that legally, and specifically, all hospitals should have a registered pharmacist on duty at all times, etc. Certainly all hospitals "retail" drugs; most hospitals "compound," though rarely; all hospitals "dispense" drugs.

Practically speaking, however, everyone concerned in Alabama feels it would be unrealistic to require all hospitals to have a registered pharmacist. There aren't enough pharmacists. And, in many cases, the small hospital could not afford a pharmacist.

Generally, the Pharmacy Board has taken a realistic view of its responsibility for enforcement. Board Secretary Gibbs puts it this way: "Since a pharmacist is not on duty at all hours, as required by Section 234 of the pharmacy act, we feel that the House Rules as provided in the permit are necessary for the protection of the patients as well as the hospital. This should not be difficult for a *pharmacist* to understand. It is conceivable that some administrators might decide that 'diet cooks,' nurses or others might be safe to take over the duties of the pharmacist during his absence. When the pharmacist and the administrator sit down to draft their House Rules relating to this, then it becomes incumbent on the pharmacist to suggest procedures that will insure availability of emergency drugs and medication during his absence from the Pharmacy. When the pharmacist is off duty, the Pharmacy should be closed. He and the administrator should spell this out in their House Rules and set out in the rules who should have a key. The person who has the key should list the emergency medication removed from the Pharmacy and turn this information over to the pharmacist when he returns to duty."

Only when a complaint has been registered with the Board has the Board, through its inspectors, exercised its legal right and responsibility to investigate, and if necessary enforce the Pharmacy Law.

The issuance in 1959 of the Special Permit for Hospital Pharmacy was a decision of the Board of Pharmacy which represents an effort to establish a more logical means of enforcing the existing Pharmacy Law. The language of the permit is short and to the point. It says that a "Registered Hospital Pharmacy (is) limited to rendering adequate pharmaceutical service to patients *residing* in the . . . Hospital subject to *House Rules* adopted by the pharmacist in charge in cooperation with the Hospital Administrator and approved by the Alabama State Board of Pharmacy. This permit is not valid for the operation of a Pharmacy or Drug Store doing an outside general prescription business as provided for under Chapter 12, Title 40, Code of Alabama, 1940."

Since only "patients residing" in the hospital are covered by the language of the permit, hospital administrators are concerned about their status in servicing their bona-fide outpatients. The Board Secretary has assured inquiring hospital administrators that this language is not intended to exclude servicing outpatients, employees and staff physicians. Nevertheless, hospital administrators are still concerned because of the "exclusiveness" of the permit.

Pharmacy Board members and hospital officials and pharmacists all are sure that, as written, the permit very definitely is aimed at preventing a hospital from doing a general prescription business in competition with the retail drug store.

Hospital officials have questioned the right of the Pharmacy Board to write this economic restraint into a professional license.

At the request of a group of hospital officials, the language of the new permit was reviewed, but the Board held firm to its language.

The "House Rules" requirement of the permit is looked upon also with mixed feelings by hospital officials. Conceivably, a set of "House Rules" relating to the handling and storage of drugs could improve patient care. Also, the hospital's policy concerning servicing outpatients could be outlined in the "House Rules." If, however, an outpatient policy for selling drugs was not "approved" by the Board, the permit would enable the Board to reject the policy. What, then, would happen?

It is too early to evaluate the impact of the new permit. In the case of the potential economic restraint directed at non-profit hospitals, the Federal Internal Revenue Department might have the last word. The position of the non-profit, partially tax-free hospital in competing with private retail business has not yet been tested, in Alabama or anywhere else.

In Alabama there are a large number of proprietary clinics and hospitals which have separate apothecaries, some inside the hospital, some adjacent. Manned (and in most cases owned) by registered pharmacists, these pharmacies are doing a big business. These are licensed as retail drug stores. There are *no* non-profit hospitals doing "general prescription businesses." In view of these facts, it is hard for hospital pharmacists and administrators to understand the Board's motivations. Secretary Gibbs explains the Board's motives this way: "The motive of the Board is simple. We think that patients residing in hospitals are entitled to adequate pharmaceutical service."

Summary

Hospital pharmacists and administrators, the Board of Pharmacy and the Board of Health have good liaison in Alabama. They do not see eye to eye on all matters, but they are talking and working together. This year, Perry Cox, Pharmacy Chief of Birmingham's Carraway Methodist Hospital, is President of the Birmingham Retail Druggists' Association, the state's largest, most influential local organization. All agree that progress is being made each year. Approximately 36 Alabama hospitals, including three Veteran's hospitals, have registered pharmacists. There are 130 licensed general hospitals in the state. A number of hospitals are actively seeking services of a full-time pharmacist. Several more have formal part-time arrangements with community pharmacists.

It would appear, then that the majority of patients, if not the majority of hospitals, have the protection of duly licensed pharmacy service.

Board of Pharmacy Secretary Elbert W. Gibbs is well liked, trusted and experienced. Both hospital pharmacists and community pharmacists respect his leadership. It is not likely that any radical laws, not ultimately in the public interest will be enacted in Alabama.

AMERICAN HOSPITAL FORMULARY SERVICE

► THE AMERICAN HOSPITAL FORMULARY SERVICE has been accepted with considerable enthusiasm and all copies of the first printing have been sold. A second printing was completed July 1, 1959. Orders may be directed to The Hamilton Press, Hamilton, Ill. The price of single copies, including supplements for one year, is $15.00.

The SOCIETY'S Committee on Pharmacy and Pharmaceuticals, working under the direction of Dr. William Heller, is preparing monographs to be included in the Supplements. It is anticipated that the Third Supplement to the Formulary Service will be available within the next month.

Subscribers will want to note that extra copies of the binder are available from The Hamilton Press at $4.00 each. Some individuals using the entire set of monographs have suggested that a second binder is helpful. Also, blank pages, for use in the Formulary Service in connection with preparing monographs not available, may be ordered from The Hamilton Press. One ream (500 sheets)) is available for $3.00; two reams (1,000 sheets) cost $5.40.

Since this is a continuing service, classifications have been included for which there are presently no monographs. It is anticipated that these will be made available in future supplements.

Suggestions or questions with regard to monographs or contents of the Formulary Service may be directed to Dr. William Heller, Chairman, Committee on Pharmacy and Pharmaceuticals, Pharmacy Department, University of Arkansas Medical Center, Little Rock, Arkansas.

Consulting WITH BOWLES

GROVER C. BOWLES JR., *Baptist Memorial Hospital, Memphis, Tennessee*

► What is a simple method for determining reasonable drug charges?

The problems of pricing in hospital pharmacy are many, varied and highly individualized. Certainly drug charges should be determined in a business-like manner and on a basis that is fair to all concerned. Professor Seymour Jeffries, formerly a member of the faculty at the Brooklyn College of Pharmacy, has suggested a method of costing and pricing prescriptions that is adaptable to hospital pharmacy. This method determines the prescription price or drug charge on the following break-down: (1) cost of ingredient, (2) cost of container, (3) cost of labor for dispensing time, (4) overhead charge and (5) professional fee. When properly calculated, the first four items give the actual cost to provide the service. To this is added the professional fee to provide the profit desired. For more information about this method of determining drug charges see: Costing and Pricing Prescriptions in the Hospital Pharmacy by S. B. Jeffries, *The Bulletin of the American Society of Hospital Pharmacists*, Nov.-Dec. 1954.

► Should the dispensing of drugs in hospitals be subject to the laws and regulations applying to retail pharmacies?

Generally speaking, I believe most hospital pharmacists feel the practice of pharmacy in hospitals should comply with the legal requirements governing the community practice of pharmacy.

► Please recommend a good pricing schedule for use in hospital pharmacy.

So far as I know, none of the twelve or fifteen pricing schedules available is suitable for use in the hospital pharmacy. The pricing problems in hospital pharmacy are complex and do not parallel those of retail pharmacy and to further complicate matters, hospitals must deal with a variety of third party paying agencies such as insurance companies and welfare agencies while the retail pharmacist deals directly with the customer or patient. It might also be pointed out that although numerous pricing schedules are available and in use, many private practitioners of pharmacy prefer to exercise their individual prerogatives in pricing prescriptions rather than conforming to a pricing schedule. Pricing schedules are not the final answer to the pricing problems of hospital or retail pharmacy and at best, should be used only as guides.

► Do you think pharmacists should allow drug pricing policies to be controlled by persons other than pharmacists?

This is a difficult question to answer without knowing more about the facts involved. Certainly the hospital administrator or for that matter, the board of trustees, would be within their rights to establish policies dealing with the charges to be made for drugs. A good administrator would undoubtedly hesitate to develop such policies without consulting the head of the department of pharmacy.

If the formulation of pricing problems is delegated to the pharmacist he should, by all means, consult with the hospital administration before making any drastic changes in existing policies and methods of pricing. The administrator is in a position to see the overall operation of the hospital and is responsible to the governing board for coordinating all activity within the institution. He must also develop budgets and live within them. The administrator is not likely to think highly of a chief pharmacist who suddenly and without warning, reduces the price of a frequently used, expensive drug which produces a significant amount of revenue unless some thought has been given about how this revenue can be replaced.

Hospital pharmacists should make every effort to be sure that all drug charges are fair, reasonable and just to all and can be honestly defended should they be questioned. As pharmacists we definitely have some professional prerogatives but let's not forget that we also have some responsibilities.

► We have considerable difficulty in getting the personnel in surgery, the labor rooms and the recovery room to account for the narcotics administered to each patient. They want to list only four or five names for each 20 ml. vial of narcotic solution. What do other hospitals do to encourage personnel working in these areas to properly account for narcotics?

Replacing the rubber stoppered vials of narcotic solutions with 1 ml. ampuls will simplify record keeping, prevent the occasional loss of a partly used vial and minimize wastage due to contamination. You might also review your accounting procedures to be sure that they are reasonable, simple and convenient. Be sure that everyone understands the accounting system and the importance of narcotic control within the hospital, even in those areas where emergencies are common and people work under pressure.

News

Provost Appointed AHFS Secretary

George Provost

MR. GEORGE PROVOST, formerly a pharmacist at University Hospital and Instructor in the School of Pharmacy at University of Arkansas Medical Center, Little Rock, has recently been appointed Secretary of the American Hospital Formulary Service, with offices at University Hospital in Little Rock. In his present position, Mr. Provost will assist Dr. William Heller, Director of the Formulary Service. This appointment, which became effective on July 1, was made following a recommendation of the ASHP Committee on Pharmacy and Pharmaceuticals and approval by the SOCIETY's Executive Committee.

Mr. Provost has already had wide experience in working with Dr. Heller during the past few years. He is a graduate of the Massachusetts College of Pharmacy and has also served as a pharmacist at the New England Medical Center, Boston, and at Mercy Hospital, Watertown, New York. He has been closely associated with the Formulary Service for the past two years and was one of the four pharmacists (others were Mrs. Gloria Francke, Paul Parker, and Joanne Branson) who spent time at The Hamilton Press during the final stage of the initial printing.

Archambault Represents PHS

PHARMACIST DIRECTOR DR. GEORGE ARCHAMBAULT has been designated to represent the U. S. Public Health Service in all pharmacy activities. Announcement of the appointment was made recently by Surgeon General Leroy E. Burney. Dr. Archambault in this staff capacity will maintain liaison with professional, educational, and industrial pharmaceutical organizations and similar associations, and will serve as advisor on pharmacy to the Surgeon General. At the same time, Dr. Archambault will continue his operational assignment as Chief of the Pharmacy Branch for the Public Health Service hospitals, a position which he has held for twelve years.

Dr. Archmabault, who is a Charter Member of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, served as President of the organization for the 1954-1955 term. He is also currently serving as a Contributing Editor of the JOURNAL.

Dr. Archambault holds Life Membership in the American Pharmaceutical Association and last year was re-elected to serve a second term on the Association's Council. He is also active in numerous other professional groups and is the author of many papers in the field of hospital pharmacy administration and jurisprudence, as well as the author of the chapter on Hospital Pharmacy Administration in Lyman and Sprowls *Textbook on Pharmaceutical Compounding and Dispensing.*

► J. ROBERT CATHCART, Secretary of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS for the 1948-1949 term, was killed in an automobile accident on August 29. A future issue of the JOURNAL will include a tribute to Mr. Cathcart who has been active in the SOCIETY for many years.

► SISTER MARY JUNILLA HASKELL, O.S.F., Treasurer of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS for the 1949-1950 term, died on August 25. Sister Junilla's contributions to hospital pharmacy and the profession will be noted in a future issue of the JOURNAL.

► EDWARD CROUMEY, Chief Pharmacist at the Mary Fletcher Hospital in Burlington, Vermont, has recently been elected Second Vice-President of the Vermont Pharmaceutical Association.

► AMERICANS WITH HEALTH INSURANCE make greater use of hospital facilities than persons who do not have such insurance, reports Health Insurance Institute.

An analysis of a June, 1958, survey by the U.S. Department of Health, Education, and Welfare shows that more than 11 of every 100 insured persons were hospitalized during the year ending September, 1956, as compared to nearly eight of every 100 uninsured persons. The average hospital stay of the insured person was 9.1 days while it was 12.8 days for the person without insurance.

1960 Institutes Scheduled

THREE INSTITUTES on hospital pharmacy have been scheduled by the American Hospital Association for 1960. These institutes are held in cooperation with the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

The first two institutes scheduled will follow the same general plan as those during previous years and will be open to all hospital pharmacists. Dates and places for these two institutes are as follows:

Ohio State University Columbus, Ohio—June 20 - 24, 1960

University of Minnesota, Minneapolis, Minnesota—August 1 - 5, 1960

News

For the first time, a Specialized Institute on Hospital Pharmacy is being scheduled and this will be held at the American Hospital Association headquarters building in Chicago, on October 10-14, 1960.

Applications, along with further details regarding the programs will be mailed to all members of the Society early in 1960.

AHA Names New Members to Joint Committee

The American Hospital Association has named two new members to the Joint Committee of the AHA and the ASHP. These individuals, who will serve for a two-year term, include Joseph Snyder, M.D., Presbyterian Hospital in the City of New York, New York, N. Y.; and Herbert A. Anderson, Lincoln General Hospital, Lincoln 2, Nebr. Other AHA representatives continuing to serve on the Committee include Robert Cadmus, North Carolina Memorial Hospital, Chapel Hill, N.C. and C. Joseph Vance, Blue Cross Commission of Alabama, Birmingham, Ala.

ASHP President Vernon O. Trygstad has re-appointed George F. Archambault, Division of Hospitals, U.S. Public Health Service, Washington, D.C.; and Grover C. Bowles, Baptist Memorial Hospital, Memphis, Tenn., to serve for two-year terms on the Joint Committee. Other ASHP representatives who continue on the Committee include Robert C. Bogash, Lenox Hill Hospital, N.Y., N.Y., and Clifton J. Latiolais, Ohio State University Health Center, Columbus, Ohio. ASHP President Vernon O. Trygstad and Secretary Gloria Francke serve on the Committee in an ex-officio capacity.

Mr. Joseph Oddis, Staff Representative of the Council on Professional Practice of the American Hospital Association serves as Secretary to the Committee and Mr. Paul Parker represents the Division of Hospital Pharmacy of the A.Ph.A. and the ASHP.

CHA Sponsors Continuing Education for Hospital Pharmacists

As a part of the Catholic Hospital Association's program on continuing education, a one week "Refresher Course" is scheduled at the Pick-Melbourne Hotel in St. Louis, October 19 to 23. This is one of a series of programs which the CHA is scheduling throughout the country. Among the subjects to be covered during this week are Basic Concepts of Inorganic Chemistry; Naming of Organic Medicinals; Relationship of Physical and Chemical Properties to Physiological Activity; Clinical Chemotherapy; Psychopharmacology; and items covering administrative activities of the hospital pharmacists.

ACA Names Hospital Fellows

The following hospital pharmacists have recently been named "Hospital Fellows" of the American College of Apothecaries: Troy L. Carter, Jr., 4925 Moore Drive, New Orleans, La.; Dudley Alvin Demarest, 908 Lyndhurst Street, Baltimore, Md.; and George W. Rowley, Josephine General Hospital, Grants Pass, Oregon.

► Hospital and Retail Pharmacists will join for a session at the Fall Pharmacy Institute at the University of Wisconsin on November 13. Speakers include ASHP President Vernon O. Trygstad who will discuss "Outpatient Dispensing from the Hospital Pharmacists' Standpoint;" Dr. William S. Apple, Secretary of the American Pharmaceutical Association will speak on "The Hospital Pharmacist's Role in the Profession;" and Louis C. Zopf, President of the American Association of Colleges of Pharmacy and Dean at the State University of Iowa School of Pharmacy, will be the luncheon speaker and discuss "Facts and Pharmacy's Future."

► The Hospital Drug Reference Book, 1959-1960, which is made available annually through McKesson and Robbins, has recently been released. According to McKesson and Robbins, this reference is the only complete drug buying guide created especially for hospital pharmacies. It contains approximately 12,000 items, which represent over 90 percent of total hospital pharmacy purchases. The reference includes an alphabetical listing which has been cross-indexed by official and generic names to make it easier to locate all brands of a given product. Improvements in the 1959-1960 *Hospital Drug Reference Book* were made as the result of helpful suggestions and criticisms by people in all phases of pharmacy and hospital administration.

A.Ph.A. House of Delegates To Meet in Washington

The interim meeting of the American Pharmaceutical Association's House of Delegates will be held in Washington, D.C., on March 27 and 28 at the Statler Hilton Hotel, according to an announcement made by J. Warren Lansdowne, Chairman of the House of Delegates. The meetings of the House are scheduled to begin at 11 A.M. on Sunday, March 27, and will adjourn at 5 P.M., Monday, March 28.

The interim meeting of the House of Delegates will be followed by the Decennial United States Pharmacopeial Convention which will be held at the Statler Hilton Hotel, Tuesday and Wednesday, March 29 and 30, with a preliminary U.S.P. conference scheduled for Monday evening, March 28.

Dr. William S. Apple, Secretary and General Manager of the American Pharmaceutical Association, said he expects an unusually large attendance at the 1960 interim meeting of the House of Delegates. There are 175 delegates to the House of Delegates, but in accordance with the by-laws of the Association, all A.Ph.A. members are invited to attend the meetings of the House and may participate in the discussions. Hotel reservation forms will be furnished to all Delegates and further announcements about the meeting will be carried in the *Journal of the American Pharmaceutical Association, Practical Pharmacy Edition.*

The interim meetings of the House of Delegates were inaugurated in 1956 and previous meetings have been held in Washington, D. C., in October or November with the exception of the 1958-59 meeting which was held in Chicago, Illinois.

► JOSEPH DESIDERIO, Chief Pharmacist at Delaware County Hospital, is the Chairman of the Poison Control Committee of the Greater Philadelphia Hospital Pharmacists' Association. In the latter capacity Mr. Desiderio has, during the past two years, spoken to all types of groups in the Philadelphia area on the cause and prevention of accidental poisoning and the establishment of Poison Control Centers. His talks have been the subject of several newspaper articles in Philadelphia.

► TEXTBOOK FOR TEACHING fundamentals in pharmacy to student nurses has been written by H.R. Mehta, Instructor in Pharmacy at the University of Colorado. The book, *Pharmacy for Nurses,* is now off the press of Delta Publishing Company (Empire Reproductions) of Boulder.

Mehta has earned degrees at the University of Bombay (India) and the University of Colorado. He served as pharmacist at Denver General Hospital and non-resident instructor at the University of Colorado extension center in Denver.

Mehta has done research on "The Study of Propylene Glycol in Some Oral Pharmaceuticals" and has written "Organic Chemistry Experiments for Nurses." He is a member of Rho Chi and Sigma Xi.

Pharmacy for Nurses, also intended for use by practicing nurses, includes such subjects as arithmetic of pharmacy, narcotics, investigational drugs, drug administration, poisons, medical terminology, drug classification and current pharmaceuticals.

► MIAMI BEACH, FLORIDA has been selected as the site for the next annual convention of the American College of Apothecaries according to an announcement made by the President of the College, Edward F. Keating. The Board of the A.C.A. selected the dates of February 14, 15, 16, 17 and current plans indicate that the meeting will be held at the Hotel Americana in Bal Harbour.

► ELI LILLY AND COMPANY, of Indianapolis, one of the world's leading pharmaceutical manufacturers, and the Syntex Corporation, internationally known research organization and producer of steroid hormones, have signed a co-operative research agreement.

Under the agreement, Lilly will share the expense of Syntex research and also will conduct clinical investigations of promising new compounds discovered in the Syntex Laboratories.

The products resulting from this research will be available for marketing by both companies.

Francke Participates in Overseas Meetings

DON E. FRANCKE, Editor of the AMERICAN JOURNAL OF HOSPITAL PHARMACY, participated in several European pharmaceutical meetings during September. In Berne, Switzerland, he met with the International Pharmaceutical Federation's Commission on Pharmaceutical Abstracts to help lay plans for issuing a journal devoted to international pharmaceutical abstracts. He also attended the International Congress of Pharmaceutical Sciences which was held in Zurich September 6 to 10. As Vice President of the International Pharmaceutical Federation, Dr. Francke attended the meeting of the FIP Council in Madrid, September 13 to 20. During his trip he also served as a pharmaceutical consultant to the World Health Organizations in Geneva. Dr. Francke attended the French Pharmaceutical Congress in Paris, September 27 to October 3.

FIP Commission on Pharmaceutical Abstracts Meets

The Commission on Pharmaceutical Abstracts of the International Pharmaceutical Federation met in Berne, Switzerland September 3 and 4, 1959. Members present included Prof. K. Steiger (Switzerland), Mr. W. K. Fitch (Great Britain), Mr. W. Eberkardt (Germany), Prof. U. Gallo (Italy), Mr. F. Milliet (Switzerland), Dr. M. Regnotto, Secretary (Switzerland), Dr. J. Winters, Secretary-General of the International Pharmaceutical Federation (Holland), Miss Winifred Sewell (U.S.) and Dr. Don E. Francke, Chairman (U.S.A.).

The Commission decided that an international pharmaceutical abstract service is desirable and agreed to investigate further the possibility of issuing a fortnightly journal containing a minimum of 6,000 abstracts per year. As one of the first steps, the Commission agreed to review the "World List of Pharma-

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ceutical Journals" compiled by Miss Sewell and to select the journals to be abstracted. The Commission also discussed in detail the estimated budget and staff required to implement the service and laid plans for a comprehensive report at the FIP meeting in Copenhagen in August 1960.

Jefferson's Pharmacy Alumni Hold Annual Reunion Luncheon

The second Annual Reunion of the Pharmacy Alumni of Jefferson Medical College Hospital, Philadelphia, Pa., was held during the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, the week of August 16, 1959, in Cincinnati, Ohio. Present were Herbert Flack, Director of Pharmacy Service at Jefferson, four Pharmacy Residents, ten former Pharmacy Residents, and four former staff pharmacists. Guests of honor were: Dr. Linwood Tice, Associate Dean at the Philadelphia College of Pharmacy and Science; Dr. Kenneth Avis, Associate Professor at that College; and Mrs. Evlyn Gray Scott, Director of Pharmacy Service at St. Luke's Hospital in Cleveland. Hospital pharmacy alumni from Jefferson Medical College Hospital number over 100, and include many pharmacists who later graduated in medicine from Jefferson. Mr. Flack is also Director of the Program in Hospital Pharmacy Administration offered jointly by the Philadelphia College of Pharmacy and Science, the Jefferson Medical College and Hospital, and the Veterans Administration Hospital of Philadelphia.

Unique Medical Film Offered by Lakeside

A novel technique in medical communications—an educational motion picture utilizing techniques developed for commercial television programs—has been incorporated by Lakeside Laboratories, Inc., in its film "A Pharmacologic Approach to the Study of the Mind."

The subject matter is of prime interest to the medical profession and the film presents in a lucid and informal manner a comprehensive review of the field. Prominent authorities in the use of chemicals to diagnose and treat mental illness report on their theories and their clinical findings.

The film borrows the TV technique made popular by Edward R. Murrow on his "Person to Person" program—in which the moderator uses an electronic picture window to bring his viewer in close contact with the subject being interviewed.

In the Lakeside film the narrator is Dr. Ralph W. Gerard, Director of Laboratories, Mental Health Research Institute, University of Michigan. The subjects are the nationally known speakers who participated in a three day symposium on "A Pharmocologic Approach to the Study of the Mind" last January in San Francisco.

The symposium was presented under the combined auspices of the University of California School of Medicine and Langley Porter Neuropsychiatric Institute.

The film was produced by Sherman H. Dryer. It is available to professional groups, upon request, from the Medical Education Department, Lakeside Laboratories, Inc., Milwaukee 1, Wisconsin.

Pharmacy Alumni from Jefferson Medical College Hospital, Philadelphia, meet in Cincinnati for annual reunion

as the president sees it—

VERNON O. TRYGSTAD, *Veterans Administration, Washington, D. C.*

► THE 1959 CONVENTION OF THE AMERICAN PHARMACEUTICAL ASSOCIATION and the ANNUAL MEETING OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS are now history—some of their excitement perhaps dimmed or forgotten, and the more pleasant aspects tucked away among memories of good times past. Resolutions and reports on the meeting were published in the JOURNAL last month. The complete proceedings, Editor Francke says, will be in the JOURNAL next month.

Thoughtful, provocative, discussions on hospital pharmacy and its relations with other branches of the profession were among the highlights of the meetings. I am convinced that these are all to the good. Certainly there will always be differences of opinion, varied interests, and conflicting viewpoints in a profession as diversified as pharmacy. Aren't there in any democracy? But in my view, the very fact that these differences are being discussed on the convention floor, in joint meetings, in panel discussions—even in heated debate—are good signs. They are signs that those who are devoted to pharmacy, and who are intensely interested in their own specialty, are big enough to receive other views in open discussion.

Hospital pharmacists are confident that their policies and practices are sound and ethical; that pharmacy is practiced on a high plane within our hospitals, with the patient way out in front as our primary interest and concern. Hospital pharmacists know this and of course would like to have all of pharmacy understand these facts. Unfortunately, it's not that simple. There are those with opposing views. Some of these are largely economic. But even though there may never be complete agreement on every issue, such differences stand their best chance of being resolved through better understanding if we review them in the open forums of the profession. We should also do our share of listening.

It is no secret that some in the pharmaceutical industry deplore the economic implications of the formulary system. It is also a fact that the generic name system is one of long established policy in many hospitals—going beyond the realm of pharmacy alone. A start has been made on discussions leading to better understanding. I believe they should be continued.

The objectives of hospital pharmacy education and internships have been discussed by representatives of colleges of pharmacy and hospital pharmacy many times—sometimes with divergent views. But these discussions finally have led to an agreement between the American Association of Colleges of Pharmacy and the ASHP to form a joint committee to work out mutual problems. This is progress.

The Forum on Pharmaceutical Services in Hospitals and Nursing Homes at the meeting of the National Association of Boards of Pharmacy probably drew as much interest and attention as any during the convention week. There was plenty of frank discussion on the regulation of pharmacy practice in hospitals, including the acceptance of hospital pharmacy internships. Certainly it was no "love feast." But it was one more important step toward the better understanding of mutual problems which must come before they can be resolved.

The National Conference of State Pharmaceutical Association Secretaries, at their Cincinnati Meeting, held discussions on hospital pharmacy practice, voicing concern over the dispensing of prescriptions to outpatients by some hospital pharmacies. This, of course, is no new issue. It is one on which many discussions have been held and definitive resolutions adopted by both the ASHP and A.Ph.A. Retail and hospital pharmacy may have some differences of opinion on hospital policies relating to the practice of pharmacy, but we would welcome and invite discussion of them. Maybe our views and interests aren't so far apart after all.

Yes, it is good that the problems of pharmacy are being discussed. The total profession of pharmacy has too much of common interest to be divided by the few remaining differences which may result from misunderstanding. Let's talk them over and find the answers.

Vernon Trygstad

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

edited by CLIFTON J. LATIOLAIS, HENRY J. DEREWICZ *and* LEO F. GODLEY

TABLETS, EFFECT OF HUMIDITY ON PREPARATION OF

Compressability and Hardness of Tablets Made of Granules with Different Humidity-Percentages, Seth, P. L. and Munzel, K., Die Pharmazeutische Industrie 21:9 (Jan.) 1959.

According to the authors, the humidity percentage of granulated material is primarily responsible for more or less successful compressing. Independently of added binders and lubricants, tablets will show the defect of capping when the granules have too low a humidity-percentage. When this percentage is too high, the tablet material will stick to the punches. In common practice, too dry materials can be wetted by spraying water on it or including glycerin in the tablet formula.

In their investigations the authors have included two types of granulated materials: (A) a hydrophilic one (Potato Starch 70, Lactose 30, Gelatin 4 percent q.s.); (B) a lipophilic or aerophilic one (Phenacetin 50, Potato Starch 75, Gelatin 4 percent q.s.). Both masses were wet-granulated and dried at 35°C in a hot air dryer. The granules were kept in five hygrostatics with different relative humidities (100-90-79-58-0 percent). After 48 hours in the hygrostate, the water-percentages were assayed by Karl Fischer titration and the materials compressed with pressures varying from 250-4000 Kg. per tablet of 6 cm. diameter. The hardness of the tablets were checked with a Monsanto-tester.

A comparison of tablets compressed with constant pressure (1000 Kg./tablet) showed that for both types of granules there exists an optimal percentage of humidity. For type A material this optimum lies at 10.5-12.8 percent of water, for type B at 3.0-3.7 percent of water.

When granules with equal humidity are compressed at different pressures, type A gives harder tablets, while type B granules, from 1000 Kg./tablet on, give a weaker tablet. This phenomenon is explained by presuming that starch in the granules acts as a water-regulator. Type A granules have a higher starch content, subsequently a higher elasticity and ability to hold water; this water forms, when present in sufficient quantity, a thin film on the tablet surface during compression, and therefore acts as a lubricant during the ejection of the tablet.

J. WOUTER HUISMAN

LYSOLECITHIN

The Physical Properties of Lysolecithin and Its Sols, Robinson, N. and Saunders, L., J. Pharm. and Pharmacol., 11:346 (June) 1959. (Department of Physical Chemistry, School of Pharmacy, University of London.)

The solubilization of triolein, cholesterol and monostearin in water by lysolecithin has been investigated by the optical density method. These substances solubilized to a considerable extent, increasing in the order—triolein, cholesterol and monostearin. An increase in temperature of 15° had little effect on solubilization of any of the three substances. The change in optical density with concentration of the solubilized component showed a similar pattern for the three substances, but the mixed sols formed had different stabilities. Lysolecithin-triolein sols contained only small proportions of triolein and were fluid and stable for no longer than 12 hours while lysolecithin-monostearin sols containing high proportions of monostearin formed gels and were stable for at least a month. Lysolecithin-cholesterol sols were unstable showing an initial rise and then a steady decrease in optical density over a period of 72 hours for given concentrations as slow separation of cholesterol was taking place. Factors operative in the solubilization of these three substances by lysolecithin have been suggested.

AUTHOR'S SUMMARY

ENTERIC COATINGS

Enteric Coatings 11, Starch (and amylose) Acetate Phthalates, Wagner, J. G., Bregnall, T. W., Long, S., J. Am. Pharm. Assoc., Sci. Ed. 48:244 (Apr.) 1959. (Product Research and Development Department, The Upjohn Company, Kalamazoo, Mich.)

Eight new whole starch (and amylose) acetate phthalates in acetyl and phthalyl contents were prepared by acetylation of a reactive form of starch or amylose with acetic anhydride in the presence of formamide followed by phthalylation of the partial acetates with phthalic anhydride in the presence of pyridine. Solubilities of the compounds indicated they would be useful substances for enteric coating. Tablets were enteric coated with one of the starch acetate phthalates and a commercial cellulose acetate phthalate. In vitro, at pH 6.9, ox bile extract but not pancreatin increased the rate of disintegration of the enteric coated tablets; hence, under these conditions, ionization of free carboxyl groups and not the actions of enzymes in pancreatin is mainly responsible for the disintegration of these enteric coated tablets.

AUTHOR'S SUMMARY

CRUDE COAL TAR OINTMENT, PARTICLE SIZE IN

Polyoxyethylene Sorbitan Esters in Ointments Containing Crude Coal Tar, Dykeman, M. and Groves, Gordon A., Can. Pharm. J., Sci. Sect. 91:240 (1958).

Of the polyoxyethylene sorbitan esters investigated, polyoxyethylene sorbitan monooleate was the most effective in reducing the particle size of crude coal tar ointments. The reduced particle size increases the therapeutic value and facilitates the removal of the ointment, thus reducing its staining characteristics.

S. P. MARINO, CHEMICAL ABSTRACTS 53,3604a

HEXACHLOROPHENE AND BITHIONOL ASSAY

Assay of Hexachlorophene and Bithionol in Solid and Liquid Soaps, Emulsions, and Dusting Powders, Van der Pol, H. J., Pharm. Weekblad, 93:881 (1958).

The best method for the determination of hexachlorophene is that of Childs and Parks (C. A. 50:10430 f). This method works well on liquid soaps but on solid soaps a turbid solution results. To overcome this, the solvent must be changed from 90% methyl alcohol to 99-100% methyl alcohol. The reagents are likewise made up in 99-100% methyl alcohol. The method is applicable for the determination of bithionol.

B. PRYTZ, CHEMICAL ABSTRACTS, 53,25391

FOLIC ACID DETERMINATION

A Folic Acid Method Involving Permanganate Oxidation, Schiaffino, S. S., Webb, J. M., Lay, H. W., and Kline, O. L., J. Am. Pharm. Assoc., Sci. Ed. 48:236 (Apr.) 1959, (Division of Nutrition, Food and Drug Administration, Department of Health, Education and Welfare, Washington, D. C.)

A chemical method for the determination of folic acid in pharmaceutical products is presented. The method involves digesting the folic acid in a mildly alkaline, buffered solution (3% K_2HPO_4) followed by splitting with $KMnO_4$, diazotizing the resulting PABA, and coupling with Bratton-Marshall reagent (n-1-naphthyl)-ethylenediamine dihydrochloride). In the presence of extraneous colored substances, as may be found in some pharmaceutical preparations, the chromogenic compound is extracted into isobutyl alcohol with no diminution in intensity of color, or change in wave length of maximal absorption (550 mu). Ferrous compounds and ascorbic acid do not interfere in the method as they are found to do in the NH_4OH digestion-zinc reduction method. The

assay time with the proposed method is less because of the shorter time required to cleave folic acid by oxidation. The results are reproducible, and good folic acid recoveries are obtained.

AUTHOR'S SUMMARY

EFFECTS OF MOUTHWASHES

The Effect of Mouthwashes on the Oral Flora, Ostrolenk, M., Weiss, W., J. Am. Pharm. Assoc., Sci. Ed. 48:219 (Apr.) 1959. (Division of Antibiotics, Food and Drug Administration, Department of Health, Education and Welfare, Washington, D. C.)

A study has been made of the efficacy of several commercial mouthwashes representing many classes of chemical agents. The method employed tends to represent, as closely as possible, the conditions of use. The selective antibacterial activity of the washes was measured in terms of "before" and "after" total bacterial counts, and the incidence of streptococci, staphylococci, fusoform bacteria, and lactobacilli. There is included a study of the length of time that elapses after the use of the mouthwashes before the number of bacteria in the oral cavity reaches the number present before washing. Data obtained from these studies indicate that each of the compounds significantly reduces the total bacterial count in the mouth and that some deal selectively with microorganisms. Each mouthwash, however, leaves residues of active bacteria among those removed from the oral cavity by a rinse technique. It appears also that the effect of the compounds is of short duration.

AUTHOR'S SUMMARY

DETERMINATION OF PHENOTHIAZINES

A New Method of Determination of Phenothiazine Compounds, Dusinsky, G., Die Pharmazie 8:478 (1958). (Journal of Pharmacy and Pharmacology 11:248 (Apr.) 1959.

A titrimetric determination of the phenothiazine compounds promethazine, diethazine, chlorpromazine and prochlorperazine is reported based on selective oxidation using either ceric sulphate or potassium bromate. A red radical is first formed by the loss of one electron, the color of which is discharged at the end point after the loss of a second electron. The progress of the titration can thus either be followed visually or electrochemically by means of a dead-stop method. With promethazine accurate results were only obtained by the dead-stop method. The method is more specific than other methods, for example, direct neutralization or determination with silicotungstic acid, since it is unaffected by the presence of alkaloidal basis, etc, for example, caffeine, amphetamine, codeine, barbituric acid derivatives and tablet excipients. The accuracy of the method is $\pm$ 1.5% for promethazine and $\pm$ 0.5% for the other compounds.

AUTHOR'S SUMMARY

EMULSIONS, HUMECTANTS IN

An Evaluation of Humectants In Cosmetic Emulsions, Henney, G. C., Evanson, R. V., and Sperandio, G. J., American Perfumer and Aromatics, 74:33 (Aug.) 1959.

Five humectant materials were evaluated as to their relative effectiveness in reducing water loss from a simple vanishing cream. Glycerol, sorbitol, propylene glycol, polyethylene glycol 400, and 1, 3 butylene glycol were added in 0.5, 10, 15, 20, and 25 percent concentrations and exposed to environments of 10-20 percent and 60-70 percent relative humidity at 30°C. for 30 days. In the lower humidity range, glycerol was effective in 5, 20, and 25 percent, while the 10 and 15 percent glycerol lost more water than a cream containing no humectant. The 5 percent concentration seems to be the most economical and was the most effective humectant evaluated in this strength. Sorbitol was effective in the 10 to 20 percent concentrations. Propylene glycol did not seem economically suitable as a humectant; however, its use may be desired for the physical property of sheen that it produces. Both polyethylene glycol and 1,3 butylene glycol produced optimum protection at a concentration of 10 percent in both humidity ranges, the latter having the additional property of producing a sheen. Rate of water loss was discussed as an important factor to consider when choosing a humectant. Physically, the hardest cream was prepared with 1,3 butylene glycol, and then polyethylene glycol the next hardest; and the softest creams were prepared by glycerol, sorbitol, and propylene glycol. No one product could be classed as the ideal humectant for all creams.

FRANZ W. GEISZ

BANANA STARCH AS DISINTEGRATING AGENT

Banana Starch as a Disintegrating Agent for Compressed Tablets, Patel, R. P., Joshi, G. J., Indian J. Pharm. 21:136 (May) 1959. (Department of Pharmaceutical Technology, L. M. College of Pharmacy, Ahmedabad, India.)

An investigation was carried out to determine the efficiency of banana starch as a disintegrating agent. The disintegration tests were performed by means of tablets composed of calcium lactate, calcium carbonate, phenacetin and phenobarbital. In order to compare the efficiency of banana starch with other common disintegrating agents, tests were also performed on tablets composed of the above medicaments and chemicals utilizing the following disintegrating agents: maize starch, Veegum and guar gum. Results indicate that banana starch is equally as effective as maize starch. Its disintegration time is also shorter than that for Veegum or guar gum. In addition, tablets prepared with these starches are glossy white, while those with Veegum and guar gum are dull and mottled in appearance.

HENRY J. DEREWICZ

ANALYSIS OF DIGOXIN

The Analysis of Digoxin Preparations, Houk, A. E. H., Alexander, T. G., and Banes, D., J. Am. Pharm. Assoc., Sci. Ed., 48:4 (Apr.) 1959. (Department of Health, Education and Welfare, Division of Pharmaceutical Chemistry.)

The authors describe a proposed assay for digoxin employing an improved *m*-dinitrobenzene reagent. The identification and purity of the glycoside are determined by chromatographic and colorimetric tests, respectively. Assays of 20 commercial preparations show the analysis applicable to crystalline powders, tablets, injections, and elixirs containing digoxin.

ROBERT W. MAHONEY

SUSPENDING AGENT

Tamarind Polyose as a Suspending Agent, Patel, R. P., Raghunathan, Y., Indian J. Pharm. 21:141 (May) 1959. (Department of Pharmaceutical Technology, L. M. College of Pharmacy, Ahmedabad, India.)

Tamarind polyose, which is mucilaginous in nature, has been studied and compared for suspending properties against several of the more commonly accepted agents. Investigation revealed that this agent is equal to, if not better than, many of the popular agents now in use.

The standard for comparison involved the settling rate of zinc oxide when suspended in different media. Actual comparison has shown that tamarind polyose, methyl cellulose and sodium alginate solutions of equal strength (1%), have approximately identical viscosities. It was noted, however, that tamarind polyose, although superior to methyl cellulose and sodium alginate in suspending property, is inferior to tragacanth and guar gum. Its suspending qualities can be more likened to that of Veegum. However, a higher concentration of Veegum (approximately five times as much) is required to obtain equivalent suspending properties.

THOMAS E. ARKINSON

CHARACTERIZATION OF TRIAMCINOLONE

Sixteen Alpha Hydroxy Steroids I: Characterization of Triamcinolone, Smith, L. L. and Halwer, M., J. Am. Pharm. Assoc., Sci. Ed. 48:348 (June) 1959.

Triamcinolone is currently marketed in this country as the alcohol, although the 16-A-, 21-diacetate has been tested clinically. Characterization of the hormone has been limited to brief accounts in the chemical journals and in the patent literature. A more detailed characterization of both triamcinolone and triamcinolone diacetate is the subject of the authors' report.

Triamcinolone and triamcinolone diacetate have been characterized by ultraviolet absorption spectra, infrared absorption spectra, absorption spectra in sulfuric acid, polarography, reduction of tetrazolium blue, and by Porter-Silber chromogens. The use of absorption spectra, polarography, and colorimetry for quantitative determination of bulk triamcinolone and triamcinolone in tablets is discussed.

Some new chemistry of 16-alpha-hydroxylated steroids is reviewed.

THOMAS E. ARKINSON

BLANKETS AND HOSPITAL INFECTION

Blankets and Hospital Infection, Schwabacher, H., Salsbury, A. J. and Fincham, W. J., Lancet 2:709 (1958).(Journal of Pharmacy and Pharmacology 11:254 (Apr.) 1959.

Two experiments were made to assess the effect of blankets on bacterial infections in hospital. The first experiment showed that the use of freshly washed blankets, disinfected with quaternary ammonium compounds, for each patient admitted to a test ward, reduced the total bacterial count (and especially the Staphylococcus aureus phage-type 80, which was previously endemic), and also decreased cross-infection. The second experiment showed a moderate reduction of the bacterial count when terylene blankets were used instead of woolen blankets. But the total bacterial count was reduced more, and there was no cross-infection, when cotton blankets were used. After the first washing, cotton blankets did not produce the fluff which seems to be a major factor in the spread of infection. It is suggested that the following measures would probably result in a great diminution in bacterial counts in hospitals: (1) woolen blankets should be replaced by cotton ones washed at 100° before use; (2) on admission, every patient should be given a bed covered with freshly washed sheets and cotton blankets; (3) all blankets should remain on the beds—ambulant patients may have separate blankets, which should be regularly washed, for use when not in bed.

AUTHOR'S SUMMARY

STABILITY OF DRUGS, PREDICTING

Stability Prediction In the Pharmaceutical Industry, Garrett, E. R., American Perfumer and Aromatics, 74:23 (Aug.) 1959.

The shelf life of many labile pharmaceutical preparations can be predicted by physiochemical and statistical procedures. Theory, statistical design, and equation based on Arrhenius' relationships are presented. It is pointed out that predictions based on some physiochemical characteristic of a labile component can save considerable time and error rather than utilizing lengthy and tedious bioassays.

FRANZ W. GEISZ

PARTICLES IN AMPULED SOLUTIONS

A Collaborative Study on the Detection of Particles in Ampuled Solutions, Graham, W. D., Chatten, L. G., Pernarowski, M., Cox, C. E., and Airth, J. M., Drug Standards 27:61 (May-June) 1959. (Food and Drug Laboratories, Department of National Health and Welfare, Ottawa, Canada.)

The problem of establishing practical standards to ensure clarity of ampuled solutions and their freedom from foreign matter has received serious consideration from regulatory bodies as well as law-enforcement agencies. The *U.S.P.* monographs are examples of attempts to establish specifications for these dosage forms. However, the detection of particles in parenteral solutions is still dependent upon the unaided human eye. The purpose of this study therefore was to determine the present status of plant inspection of ampuls, to learn something of the factors which may influence the adequacy of inspections, and to determine whether or not individual inspectors, with relatively little and sporadic experience, could perform an adequate inspection of ampuls to detect the presence of extraneous particles. This was accomplished by a series of inspections of both accepted and rejected ampules supplied by three drug manufacturers. Inspections were performed by inspectors with varied amounts of experience ranging from no experience to inspectors with more than 10 years of experience. In addition, the conditions under which the inspections were carried out were varied in order to note the variable results possible with unusual viewing conditions.

Results of the investigation indicate that: (a) in the inspection of ampuls, containing clear, aqueous solutions, for freedom from extraneous particles, 12 individual inspectors agreed with their own previous decisions, as to whether or not an ampul should be rejected, 64 to 83 percent of the time; (b) generally, an inspector who found a high percentage of rejects usually found it more difficult to obtain a high level of self-agreement, presumably because many of the particles found were at the limits of detection; (c) trained and experienced inspectors worked at a faster rate and found two-thirds more rejects than inexperienced inspectors; (d) comparison with rejects originally claimed by the manufacturers revealed that, on the average, the untrained inspectors found 18 percent more than claimed, and all other inspectors 25 percent less than claimed; (e) no evidence was obtained to support the belief that, over a prolonged period, the number of reject ampuls in a given lot increases; and (f) the 10 ml. size ampul had the smallest number of rejects and the 1 ml. size the largest number of rejects.

HENRY J. DEREWICZ

OPTICAL CRYSTALLOGRAPHY

The Optical Crystallographic Properties of the Xanthyl Derivatives of Some Barbiturates, Julian, E. A. and Plein, E. M., J. Am. Pharm. Assoc., Sci. Ed. 48:207 (Apr.) 1959. (College of Pharmacy, University of Washington, Seattle, Wash.)

The optical crystallographic properties of the xanthyl derivatives of 14 commonly used barbiturates and the micro-melting points of these same derivatives and 5 additional ones are presented. The crystallographic properties, especially the three principal indexes of refraction, readily serve to identify the compounds in question. The crystallographic properties are of particular value when the melting points of the derivatives are close in range.

AUTHOR'S SUMMARY

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

ADMINISTRATION

—Costs

Moravec, D. F. and Reinert, Carroll R.: A Simple Method of Determining Injection Costs, Part I, *Hosp. Management* 88:88 (Sept.) 1959; Part II, 88:84 (Oct.) 1959.

—Workloads

Kitchen, J. B.: Work Study in Hospitals, *Public Pharmacist* (Great Britain) 16:176 (July) 1959.

EDUCATION

Mohan, Thomas Jr.: Integrated Methods of Teaching, *Hosp. Progress* 40:112 (Sept.) 1959.

INTERNATIONAL

Benfante, Paule: Impressions of the I.P.F. Conference, Brussels, September, 1958, *Hosp. Pharm.* (Canada) 12:170 (July-Aug.) 1959.

LAWS AND REGULATIONS

Benfante, Paule: Laws Governing the Hospital Pharmacist, *Hosp. Pharm.* (Canada) 12:169 (July-Aug.) 1959.

Anon.: Trade Name on Label Must Be That of the Brand Dispensed, *Am. Druggist* 140:20 (Sept. 7) 1959.

MANUFACTURING

Williams, A. R.: Small Scale Tablet Manufacture, *Public Pharmacist* (Great Britain) 16:168 (July) 1959.

PHARMACY AND THERAPEUTICS COMMITTEE

—Formulary System

Vance, Joe: The Formulary System and the Principle of Prior Consent, *South. Hosp.* 27:58 (Sept.) 1959.

PARENTERAL SOLUTIONS

Sykes, C. H.: Some Intravenous Transfusion Solutions for Special Purposes, *Public Pharmacist* (Great Britain) 16:178 (July) 1959.

PROFESSIONAL RELATIONS

Johnson, A. C.: Mixed in the Mortar, *Hosp. Pharm.* (Canada) 12:167 (July-Aug.) 1959.

Teplitsky, Benjamin: A Survey of Hospital Nursing as Viewed by the Nursing Service, *Am. J. Hosp. Pharm.* 131:174 (May) 1959.

STANDARDS

Anon.: Check List for Periodic Rating of Pharmacy Service, *Hospitals* 33:91 (Sept. 1) 1959.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include some of those published in the *A.M.A. Journal* for June 27, July 4 and July 11. Additional monographs for June 27, July 18, and July 24 appeared in the October issue of THIS JOURNAL.

Notice

New and Nonofficial Drugs 1959 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1959 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to January 1, 1959. The indexes listed below contain those drugs evaluated and published between December 20, 1958 and July 25, 1959*

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*Some of the drugs evaluated and Council Reports included in the June 27, July 18, and July 25 issues of the *A.M.A. Journal* appeared in the September issue of THIS JOURNAL.

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REPORT TO THE COUNCIL

The Council has authorized publication of the following paper, which was presented as part of a symposium-panel discussion held in Washington, D. C., Sept. 25, 1958, on the Use and Abuse of Adrenal Steroids. This is the fourth paper in the series, the first three of which appeared in THE JOURNAL *on June 20 and 27 and July 4, 1959, pp. 952, 1063, and 1179.*

H. D. KAUTZ, M.D., *Secretary.*

STEROID THERAPY IN SKIN DISORDERS

RICHARD B. STOUGHTON, M.D., CLEVELAND

One of the most useful agents introduced for topical dermatological therapy in the past 20 years has been hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) and some of its derivatives. There are currently well over 50 marketed topical preparations which contain one of these adrenal steroids. It would be a fair guess that 10 million containers of steroids were dispensed last year for the topical treatment of skin diseases, not to mention countless pills, solutions, and suspensions of steroids for oral, intramuscular, intravenous, and intracutaneous administration.

The vast majority of patients with skin diseases who receive steroids use the steroids in topical preparations. The topical use of steroids has been of great advantage. Used in this way, there are rarely any systemic side-effects, and the patient requires far less supervision than when the steroids are given orally.

As with any other disease for which steroids are used, skin disorders are controlled but not cured by these compounds. Almost without exception, use of steroids is only one of many important factors necessary to successfully manage a given skin disease. As many physicians have painfully learned, it is extremely difficult to adequately control the vast majority of skin diseases with steroids alone, even if there may be some response to steroids at some time during the disease. Unfortunately, it is still necessary to obtain a detailed history, perform extensive diagnostic procedures, and make a proper diagnosis before any attempt to use steroids can be considered. Contrary to many opinions, the introduction of steroids to dermatology has complicated rather than simplified the management of dermatoses. It is the understanding of the complexities of skin diseases which enables one to use steroids wisely to the advantage of the patient rather than to use them in ignorance to the disadvantage of the patient.

It is not the purpose of this paper to review all clinical studies that have been made on the use of steroids in skin diseases but rather to condense the results of the more exhaustive studies. Concentration will be on the use of steroids by topical application or by intracutaneous injection.

Director of Dermatology, Western Reserve University.

Obviously, many skin diseases, particularly the eczematous group, will respond to systemic or topical administration. Other skin diseases, such as those associated with systemic collagen diseases, pemphigus vulgaris, sarcoidosis, drug eruptions, and urticaria, may respond to systemic steroid therapy but not to topical therapy.

The great majority of reports on the clinical use of steroids by topical and intracutaneous administration have appeared in publications in the United States. They have been concerned primarily with cortisone (Cortisone, Cortogen, Cortone) acetate, hydrocortisone, fludrocortisone (Alflorone, F-Cortef, Florinef) acetate, prednisolone (Delta Cortef, Hydeltra, Meticortelone, Meti-Derm, Paracortol), and water-soluble hydrocortisone in various concentrations, in various vehicles, and with various added medicaments, particularly the antibiotics.

Cutaneous Absorption and Metabolism of Steroids

Paramount to understanding the action of steroids applied topically is a knowledge of how and in what quantities they penetrate the skin after they are applied to the surface. Early studies suggested that steroids were not absorbed through the skin or at least did not provoke any physiological evidence of their absorption.[1] However, it was soon clearly shown that fludrocortisone was absorbed through the skin in sufficient concentrations to give such systemic side-effects as depression of circulating eosinophils, urinary 17-ketosteroids, and urinary sodium, as well as induction of edema and weight gain.[2] Later it was shown, with tracer techniques, that hydrocortisone and cortisone were absorbed through normal skin and that, quantitatively, about 1% of the applied steroid was absorbed and excreted in the urine.[3] Malkinson[4] also demonstrated that damaging the skin by removing its superficial barrier will allow up to 75% of the steroid to pass through the skin. This variability in percutaneous absorption, which depends on the extent of cutaneous damage, explains, in part, why there is such a variation in response of given skin diseases at different times in the same person or from one person to another.

Significant contributions have been made to the problem

of the metabolism and fate of steroids which are introduced into the skin.[5] Malkinson and associates have shown that the skin converts hydrocortisone to cortisone (or a very similar compound) and cortisone to hydrocortisone. Cortisone is more rapidly metabolized in skin than is hydrocortisone. Prednisone (Deltasone, Deltra, Meticorten, Paracort) and prednisolone were metabolized very slowly, if at all, after nine hours' incubation with skin.[5a] Goldman and his group have shown that water-insoluble steroids, when injected into human skin, remain in situ for extended periods of time and cause rather characteristic histological changes in the areas of injection.[5] It is known that water-soluble steroids have little, if any, clinical effect when injected intradermally, as compared to hydrocortisone. This is probably because of the rapid absorption of the water-soluble steroid from the injection site.[7]

Mode of Action of Steroids

The provocative question of "how do steroids work?" has not been answered for skin diseases any better than it has for most other diseases in which steroids have such a striking effect. There have been well over 1,000 reports concerning specific physiological and pathophysiological effects of steroids in animals and man. An excellent review has been presented by Noble.[8] However, none of these studies has given a satisfactory insight to the mechanism of action of steroids in skin diseases. Unfortunately, we are still stuck with the grossly inadequate phrase of "anti-inflammatory" to glorify our ignorance in this question.

A few of the numerous interesting effects of steroids should be included in this report because of their possible application to clinical observations. The list, which includes only a small minority of observed physiological and pathophysiological alterations induced by steroids,[9] is as follows: (1) inhibition of delayed allergic reactions; (2) in vitro inhibition of proteolytic epidermolysis; (3) inhibition of leukotoxin activity; (4) decrease in biological response to tuberculin, lepromin, iodiomycin, poision ivy antigen, histamine, Frei antigen, and Ducrey antigen; (5) atrophy of sebaceous glands (rat); (6) increased incidence of experimentally induced tumors (mice); (7) decrease in mitotic activity of the epidermis; (8) decrease in Shwartzman reaction; (9) suppression of anaphylaxis; (10) antipyretic activity; and (11) depression of the basic inflammatory response, i. e., decrease in vasodilatation, stickiness of cells to vessel wall, diapedesis, and exudate. Despite such fundamental observations and the phenomenal versatility of steroids in altering physiological functions, there is no solid base for explaining the mechanism of action of steroids in skin diseases.

Clinical Use of Steroids

The first consideration in the clinical use of steroids in skin diseases is to determine what diseases are improved by their use and in what form (oral, intracutaneous, topical) they are used to best advantage. The table summarizes many reports in an attempt to outline the answer to this question.[10] Obviously, for most of these skin diseases, other therapeutic measures are as important or even more important in their management.

Most skin lesions that respond to topical application of steroids will also respond to oral or intracutaneous injection of the steroid. However, many skin diseases which respond to oral or intracutaneous administration will not respond to topical application. There are some skin lesions which will respond to intracutaneous injection of steroids but not to either oral or topical use. For the most part, these differences are best explained on the basis of concentration of the steroid in the area in which it is needed. The concentration needed locally, if attained by systemic administration, will usually lead to severe systemic complications if continued over a prolonged period of time. Intracutaneous use has led to practically no systemic complications because of the concentration of this form of therapy on small lesions. However, intracutaneous injection may lead to local atrophy or even sensitization by an ingredient in the suspension other than the steroid.[10v] These complications are reversible and with due caution should not seriously interfere with the judicious use of steroids administered intracutaneously.

Some workers have shown that mild systemic side-effects are possible from the topical use of fludrocortisone. However, systemic effects from topical use of hydrocortisone or prednisolone, even over large areas for long periods of time, are practically nonexistent.

The danger of local infection in areas treated topically with steroids is minimal, except for herpes simplex, which may spread alarmingly in the presence of steroid therapy. It has been somewhat surprising to dermatologists that secondary infection induced by steroid therapy has been so rare, particularly in view of the warnings that were initially given after experience with severe spreading bacterial lesions provoked in other organs by the systemic administration of steroids.

The use of antibiotics incorporated in steroid ointments and lotions as a preventive measure seems to have but little justification in the vast majority of cases. If a skin disease for which a topically administered steroid is indicated is secondarily infected, it would seem wise to treat the lesion with a steroid combined with an antibiotic.[10w]

In spite of the large number of reports on the topical use of various steroids, there are relatively few experiments which are well controlled throughout. The studies which have been carefully done indicate that hydrocortisone is as good as any of the steroids, if not superior to them.[11] Fludrocortisone, in one-tenth the concentration of hydrocortisone, is probably as effective as hydrocortisone[12] but does have the remote yet definite disadvantage of systemic side-effects.[10o] Water-soluble hydrocortisone seems to be as good as water-insoluble hydrocortisone,[13] and prednisolone may be slightly inferior to hydrocortisone.[14] These different steroids are used in variable concentrations, which may partly explain slight variations in effect among hydrocortisone, fludrocortisone, water-soluble hydrocortisone, and prednisolone. New derivatives of steroids are now being tested for their topical effects in skin diseases. As yet there is no definite evidence that they are superior to those mentioned previously.

In general, the higher the concentration of the steroid at its application site the more beneficial it will be. Frequently, the difference in response between a 1% and a 2.5% concentration of hydrocortisone is not significant enough to justify the added expense. The same fundamental also applies to intralesional injection of steroids. It is wise to use the smallest possible concentration of steroids intracutaneously because of the unpleasant complication of atrophy of the skin at the injection site with higher concentrations. It might be added that cortisone is useless when applied topically,[15] but it is fortunate that topical steroid therapy was not abandoned on the basis of this initial experience.

The base in which the steroid is incorporated seems to make some difference in therapeutic effect.[16] In general, the bases used are primarily three types: (1) greasy or hydrophobic, (2) creams or hydrophilic, (3) lotions. In wet, oozing lesions the lotions are more satisfactory, and in intertriginous areas the creams and lotions are more satisfactory than the greasy bases. However, for most skin lesions in most areas the hydrophilic bases seem slightly superior. It is difficult to state any generalities about choice of a base, and it usually requires the intuition of an experienced dermatologist to pick the right type of base for any given lesion.

More steroids applied topically are probably used in treating eczematous diseases of the skin than all the other skin diseases combined. This is understandable when one considers that about 25% of all patients treated by dermatologists have an eczematous disease and that most of the eczematous diseases are improved by the topical use of steriods. There is some debate as to whether steroids applied topically are of any value in allergic contact dermatitis.[17] In severe cases,

certainly, the oral use of steroids has a dramatic effect. The greatest benefit of the topical use of steroids in eczematous eruptions probably is experienced in atopic dermatitis and related diseases such as infantile eczema, dyshidrosis, housewife's eczema, and neurodermatitis. The topical use of steroids alone is hardly worthwhile, however, unless the other important therapeutic factors in this disease group are incorporated in the treatment regimen. Long-term topical use of steroids in most of the eczematous diseases has real advantages; however, this means daily application of steroids for many weeks and even months after visible signs of the disease have disappeared.

The oral use of steroids in eczematous diseases should be discouraged as much as possible. These diseases are chronic, recurrent, and persistent. Prolonged management with steroids given orally frequently leads to unpleasant, if not drastic, side-effects. Usually the dose level for control of the disease increases as time goes on. All too frequently, after two to three years of oral steroid therapy, the physician has to tell his scratching, eczematous, unhappy "Cushingoid" patient that the oral medication must finally be stopped and that he must now try to get along on steroids applied topically and other forms of management. Too many such patients are given oral steroid therapy for the following unjustifiable reasons: (1) to impress the patient with a dramatic initial response, (2) to obviate having to explain the details of the disease to the patient and the complicated factors in its course and management, and (3) because of ignorance of the other important and effective methods of control of this disease group. Only the most severe, extensive, recalcitrant eczematous eruptions present occasional legitimate grounds for the oral use of steroids.

Uses of Adrenal Steroids in Skin Diseases

	Route of Administration		
	Oral	Intracutaneous	Topical
	Response*		
Disease			
Alopecia areata	Good	Good	None
Anogenital pruritus	Good	Good	Good
Atopic dermatitis	Good	Good	Good
Chondrodermatitis nodularis chronica helicis	----	Good	None
Contact dermatitis	Good	Good	?
Dermatitis herpetiformis	Good	----	None
Dermatomyositis	?	----	None
Drug eruptions	Good	----	None
Erythema multiforme	Good	----	None
Granuloma annulare	----	Good	None
Kaposi's sarcoma	None	----	----
Lichen planus	?	Good	None
Lichen vidal	?	Good	?
Localized myxedema	----	Good	None
Lupus erythematosus	Good	Good	None
Lymphomas	Good	Good	None
Mycosis fungoides	Good	Good	None
Necrobiosis lipoidica diabeticorum	----	Good	None
Nummular eczema	Good	Good	Good
Pemphigoid	Good	----	None
Pemphigus vulgaris	Good	----	None
Periarteritis nodosa	Good	----	None
Pityriasis lichenoides et varioliformis acuta	Good	----	None
Postherpetic neuralgia	?	----	None
Psoriasis	?	Good	None
Pustular bacterid	----	----	None
Pyoderma gangrenosum	?	----	None
Sarcoidosis	Good	Good	None
Scleroderma	?	----	None
Solar urticaria	None	----	None
Synovial cysts	----	Good	None
Urticaria	Good	----	None
Xanthoma	----	Good	None

*---=Insufficient data; ?= variable response.

There is a justifiable growing interest in the use of steroids in suspension for intracutaneous injection. This method, of course, is confined to relatively small lesions which are few in number. Examples of such lesions in which intracutaneous administration of steroids presents real advantages are sarcoidosis, necrobiosis lipoidica diabeticorum, granuloma annulare, lichen vidal, synovial cysts, xanthomas, keloids, localized myxedema, resistant plaques of discoid lupus erythematosus, and hypertropic lichen planus (see table). Most interesting is the realization that such a large number of dermatoses can be suppressed by steroids if the local concentration is high enough. One hopefully awaits the topically applied steroid which will pass easily into the skin and remain in the skin for prolonged periods of time.

Orally administered steroids have been extremely useful in managing acute urticaria, various drug eruptions, pemphigus vulgaris, pemphigoid, and erythema multiforme. Steroids given orally will regrow hair in alopecia areata, but they should be given only to highly selected cases, if at all. It is generally agreed that disseminated lupus erythematosus and periarteritis nodosa are dramatically controlled, as a rule, with orally administered steroids, but other diseases of the "collagen disease group" such as scleroderma and dermatomyositis have not responded particularly well to oral administration.

References

1. Smith, C. C.: Urinary Excretion of 17 Ketosteroids and 17 Hydroxycorticosteroids After Inunction of Hydrocortisone Ointment: Attempts to Demonstrate Systemic Absorption from Topically Applied Hydrocortisone Ointment, J. Invest. Dermat. *25*:67-69 (July) 1955; Eosinophilic Response After Inunction of Hydrocortisone Ointment: Experiments Demonstrating Lack of Significant Absorption and of Systemic Effects, A. M. A. Arch. Dermat. & Syph. *68*:50-53 (July) 1953. Danto, J. L., and Maddin, S.: Eosinophilic Response in Normal Subjects Following Inunction of Cortisone Ointment, J. Invest. Dermat. *18*:381-384 (May) 1952.

2. Livingood, C. S.; Hildebrand, J. F.; Key, J. S.; and Smith, R. W., Jr.: Studies on Percutaneous Absorption of Fludrocortisone, A. M. A. Arch. Dermat. *72*:313-327 (Oct.) 1955. Fitzpatrick, T. B.; Griswold, H. C.; and Hicks, J. H.: Sodium Retention and Edema from Percutaneous Absorption of 9-Alpha-Fluorohydrocortisone Acetate Lotion and Ointment, to be published.

3. Malkinson, F. D.; Ferguson, E. H.; and Wang, M. C.: Percutaneous Absorption of Cortisone-4-C^{14} Through Normal Human Skin, J. Invest. Dermat. *28*:211-216 (March) 1957. Malkinson, F. D., and Ferguson, E. H.: Percutaneous Absorption of Hydrocortisone-4-C^{14} in Two Human Subjects, ibid. *25*:281-283 (Nov.) 1955.

4. Malkinson, F. D.: Studies on Percutaneous Absorption of C^{14} Labeled Steroids by Use of Gas-Flow Cell, J. Invest. Dermat. *31*:19-28 (July) 1958.

5. (*a*) Goldman, L.: Histological Effects of Hydrocortisone in Skin of Man, Ann. New York Acad. Sc. *61*:520-533 (May 27) 1955. (*b*) Malkinson, F. D.; Lee, M. W.; and Cutakovic, I.: In Vitro Studies of Adrenal Steroid Metabolism in Skin, read before the Society for Investigative Dermatology, San Francisco, June 22, 1958.

6. (*a*) Goldman, L., and others: Studies in Local Action of Corticosteroids at Cellular Level in Skin of Man, J. Invest. Dermat. *29*:1-6 (July) 1957. (b) Goldman, L.; Preston, R. H.; and Basket, J.: Local Intralesional Injection of Hydrocortisone with Cartridge Type of Syringe, A. M. A. Arch. Dermat. *71*:157 (Feb.) 1955. (*c*) Goldman, L.; O'Hara, E. H.; and Baskett, J.: Study of Local Tissue Reactions in Man to Cortisone and Compound F: Histopathological Studies of Local Effect of Compound F in Normal and Pathologic Skin of Man, J. Invest. Dermat. *20*:271-283 (April) 1953. (*d*) Atkinson, W. B.; Suskind, R. R.; and Goldman, L.: Reaction of Normal Human Skin to Intra-

dermally Injected Hydrocortisone, A. M. A. Arch. Path. *62*:8-13 (July) 1956.

7. Goldman, L., and Barnett, S. M.: Failure of Soluble Prednisolone Hemisuccinate to Inhibit Local Inflammation on Local Injection, J. Invest. Dermat. *28*:269-270 (April) 1957.

8. Noble, R. L.: Physiology of Adrenal Cortex, in The Hormones: Physiology, Chemistry and Applications, edited by G. Pincus and K. V. Thimann, New York, Academic Press, Inc., vol. 3, 1955.

9. (*a*) Bullough, W. S.: Stress and Epidermal Mitotic Activity: Effects of Adrenal Hormones, J. Endocrinol. *8*:265-274 (July) 1952. (*b*) Smith, D. J.: In Vitro Demonstration of Antihistaminic Action of Cortisone, Fed. Proc. *10*:249 (March) 1951. (*c*) Menkin, V.: Effects of ACTH on Mechanism of Increased Capillary Permeability to Trypan Blue in Inflammation, Am. J. Physiol. *166*:518-523 (Sept.) 1951. (*d*) Ebert, R. H., and Barclay, W. R.: Changes in Connective Tissue Reaction Induced by Cortisone, Ann. Int. Med. *37*:506-518 (Sept.) 1952. (*e*) Marcus, S., and Donaldson, D. M.: Suppression of Shwartzman Phenomenon by Adrenocorticotropic Hormone and Cortisone: Quantitative Aspects, J. Immunol. *69*:101-108 (July) 1952. *(f)* Hitch, J. M.: Action of Cortisone on Skin of Experimental Animals: Investigations on Protection Against Several Types of Injury to Skin, A. M. A. Arch. Dermat. *68*:256-265 (Sept.) 1953. (*g*) Haskin, D.; Lasher, N.; and Rothman, S.: Some Effects of ACTH, Cortisone, Progesterone and Testosterone on Sebaceous Glands in White Rat, J. Invest. Dermat. *20*:207-212 (March) 1953. (*h*) Piccagli, R., and others: On Development of Epidermal Methyl-cholanthrene Tumors in Mice Receiving Cortisone, ibid. *22*:317-333 (April) 1954. (*i*) Appel, B.; Fernandez, J. M. M.; and Dougherty, E. F.: Influence of Local Injection of Hydrocortisone (Compound F) on Reactions to Tuberculin, Lepromin, Frei and Ducrey Antigens, ibid. *23*:237-250 (Oct.) 1954. (*i*) Haxthausen, H.: Some Experiments with Electrophoretic Patch Tests, ibid. *24*:211-216 (March) 1955. (*k*) Nilzen, A.: Some Endocrine Aspects of Skin Sensitization and Primary Irritation: Observation on Influence of Cortisone on Cutaneous Irritation and Sensitization Induced by Various Chemical Compounds, ibid. *18*:7-35 (Jan.) 1952. (*l*) Baldridge, G. D., and Kilgman, A. M.: Effect of Cortisone on Experimentally Induced Contact Dermatitis, ibid. *17*:257-259 (Nov.) 1951. (*m*) Frank, L.: Study of Antipruritic Effects of Topical Steroids, A. M. A. Arch. Dermat. *77*:433-434 (April) 1958. (n) Scott, A.: Study of Action of Chymotrypsin on Skin, J. Invest. Dermat. *30*:201-205 (April) 1958. Reference 8.

10. (*a*) Robinson, R. C. V.: Use of Fludrocortisone Acetate in Dermatoses, J. A. M. A. *157*:1300-1302 (April 9) 1955. (*b*) Tolman, M. M.: Case Presentation: Mycosis Fungoides: Remission Following Steroid Therapy, A. M. A. Arch. Dermat. *75*:146-147 (Jan.) 1957. (*c*) Domonkos, A.: Hypertrophic Lichen Planus Treated by Local Injection of Prednisolone, ibid. *75*:264-265 (Feb.) 1957. *(d)* Case Presentation: Alopecia Areata (Totalis): Results of Prednisolone Local Injections, ibid. *75*:461-462 (March) 1957. (*e*) Asboe-Hansen, G.; Brodthagen, H.; and Zachariae, L.: Treatment of Keloids with Topical Injections of Hydrocortisone Acetate, ibid. *73*:162-165 (Feb.) 1956. (*f*) Savitt, L. E.: Injection of Hydrocortisone into Dermatologic Lesions, ibid. *76*:780-782 (Dec.) 1957. (*g*) Aaron, J. N.; Kantor, I.; and Stromeyer, H.: Vibra-puncture Technique in Treatment of Localized Neurodermatitis, ibid. *77*:576-580 (May) 1958. (*h*) Forsey, R. R., and Anhalt, A. W.: Hydrocortisone in Treatment of Localized Myxedema, ibid. *74*:352-354 (Oct.) 1956. (*i*) Smith, J. G., Jr.: Necrobiosis Lipoidica, ibid. *74*:280-285 (Sept.) 1956. (*j*) Sullivan, R. D.; Mayock, R. L.; Jones, R., Jr.; and Beerman, H.: Local Injection of Hydrocortisone and Cortisone into Skin Lesions of Sarcoidosis, J. A. M. A. *152*:308-312 (May 23) 1953. (*k*) Epstein, E.: Silica Granuloma of Skin, A. M. A. Arch. Dermat. *71*:24-35 (Jan.) 1955. (*l*) Malkinson, F. D., and Wells, G. C.: Adrenal Steroids in Periarteritis Nodosa: Review of Therapeutic Results with Case Report, ibid. *71*:492-499 (April) 1955. (*m*) Sauer, G. C.: Herpes Zoster: Treatment of Postherpetic Neuralgia with Cortisone, Corticotropin, and Placebos, ibid. *71*:488-491 (April) 1955. (*n*) Fergusson, A. G.; Dewar, W. A.; and Milne, J. A.: Steroid Therapy in Reticulosis of Skin with Special Reference to Exfoliative Dermatitis, Brit. J. Dermat. *70*:58-64 (Feb.) 1958. (*o*) Steiner, K., and Frank, L.: Clinical Experiences with Cortisone and Corticotropin (ACTH) in Some Cutaneous Diseases, A. M. A. Arch. Dermat. *65*:524-534 (May) 1952. (*p*) Ferguson, B. C.; Rosenbaum, J. D.; and Tolman, M. M.: Cortisone and Corticotropin in Treatment of Diseases of Skin, ibid. *65*:535-542 (May) 1952. (*q*) Stoughton, R. B.: Long-term Management of Pemphigus Vulgaris with Corticotropin (ACTH), J. A. M. A. *160*:1011-1014 (March 24) 1956. (*r*) Hopkins, J. G., and others: Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone in Diseases of Skin: Allergic and Other Dermatoses: Report of 67 Cases, A. M. A. Arch. Dermat. *65*:401-421 (April) 1952. (*s*) Frazier, C., and others: Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on Several Varieties of Pemphigus, J. Invest. Dermat. *17*:55-60 (Aug.) 1951. *(t)* Dillaha, C. G., and Rothman, S.: Treatment of Alopecia Areata Totalis and Universalis with Cortisone Acetate, ibid. *18*:5-6 (Jan.) 1952. (*u*) Eskind, I. B.; Sigafoos, R. B.; and Kelso, R. W.: Treatment of Rhus Dermatitis with Topical Hydrocortisone: Clinical Evaluation, A. M. A. Arch. Dermat. *69*:410-413 (April) 1954. (*v*) Heilesen, B.; Kristjansen, A.; and Reymann, F.: Hydrocortisone in Therapy of Cutaneous Disease: Preliminary Report, ibid. *70*:360-362 (Sept.) 1954. (*w*) Robinson, H. M., Jr.; Strahan, J. F.; and Robinson, R. C. V.: Treatment of Dermatoses with New Steroid (Ethamicort), Antibiotic Med. *3*:461-465 (Dec.) 1956. (*x*) Stoughton, R. B.: Unpublished data. Reference 6*a*.

11. (*a*) Sulzberger, M. B.; Whitten, V. H.; and Smith, C. C.: Hydrocortisone (Compound F) Acetate Ointment in Dermatological Therapy, J. A. M. A. *151*:468-472 (Feb. 7) 1953. (*b*) Frank, L.; Stritzler, C.; and Kaufman, J.: Hydrocortisone (Compound F) Free Alcohol and Hydrocortisone Acetate for Topical Use: Clinical Evaluation, A. M. A. Arch. Dermat. *71*:117-120 (Jan.) 1955. (*c*) Frank, L., and Stritzler, C.: Prednisolone Topically and Systemically: Clinical Evaluation in Selected Dermatoses: Preliminary Report, ibid. *72*:574-549 (Dec.) 1955. *(d)* Smith, C. C.: Prednisolone Ointment and Hydrocortisone Ointment, ibid. *74*:414-415 (Oct.) 1956. *(e)* Reference 10*a*.

12. Frank, L.: Hydrocortisone Diethylaminoacetate: Water-soluble Hydrocortisone Ester: Preliminary Report, A. M. A. Arch. Dermat. *75*:876 (June) 1957.

13. References 10*w* and 12.

14. Reference 11*c* and *d*.

15. Goldman, L.; Thompson, R. G.; and Trice, E. R.: Cortisone Acetate in Skin Disease: Local Effect in Skin from Topical Application and Local Injection, A. M. A. Arch. Dermat. *65*:177-186 (Feb.) 1952.

16. Kalz, F., and Scott, A.: Hydrocortisone Ointment Bases: Clinical Evaluation of Effect of 11 Different Vehicles Containing 1 Percent Hydrocortisone, A. M. A. Arch. Dermat. *73*:355-360 (April) 1956.

17. References 6*c* and 9*j*, *k*, and *l*.

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REPORT TO THE COUNCIL

The Council has authorized publication of the following paper, which was presented as part of a symposium-panel discussion held in Washington, D. C., Sept. 25, 1958, on the Use and Abuse of Adrenal Steroids. This is the second paper in the series, the first of which appeared in THE JOURNAL *on June 20, 1959, page 951.*

H. D. KAUTZ, M.D., *Secretary.*

STEROID THERAPY IN RHEUMATOID DISEASES

L. MAXWELL LOCKIE, M.D., Buffalo

Ten years have elapsed since cortisone (Cortisone, Cortogen, Cortone) acetate was first given to a patient with rheumatoid arthritis. This occurred on Sept. 21, 1948, at the Mayo Clinic under the direction of the team composed of Drs. Hench, Kendall, Slocumb, and Polley.[1] Spearheaded by the immediate spectacular changes in the symptomatology of rheumatoid arthritis, there resulted a great increase in interest in the field of rheumatic diseases, with expanded research and improved care for the arthritic patients. Also, as a result, there has been a search for better understanding of the underlying immunological and pathological states in these diseases.

This discussion concerns rheumatoid diseases which include gout, acute rheumatic fever, rheumatoid spondylitis, collagen or connective tissue diseases, and rheumatoid arthritis.

Gout and Gouty Arthritis

Adrenal cortical steroids have been used orally in the treatment of acute attacks of gouty arthritis since 1949, with varying grades of effectiveness. In some patients the results were excellent, but in other patients only a mild degree of improvement was obtained. Because of lack of uniformity of relief of acute gouty arthritis, the adrenal steroids have not been used routinely. However, recently in our experience, a combination of 0.5 mg. of colchicine with 8 mg. of triamcinolone (Aristocort, Kenacort) taken every two hours for four doses has been consistently effective. This is repeated the following day only if necessary. Complete relief of pain and swelling has occurred in all acute attacks. No untoward reactions or side-effects to either drug have been observed.

Although corticotropin (ACTH, Acthar, Corticotropin) is not an adrenal steroid, it stimulates their production and should be discussed. It has been used with uniformly satisfactory results in the treatment of the acute attack of gouty arthritis. A dose of 40 to 60 U. S. P. units intramuscularly two or three times a day for several days, or a single injection of 100 to 120 U. S. P. units of purified corticotropin (ACTH, Purified; Depo-ACTH; Purified Corticotropin) gel, or the intravenous use of 20 to 40 units has been effective. This method is used in those who are unable to take medicaments by mouth such as the patient after operation as well as those who seek treatment when oral therapy has been ineffective, as in a particularly difficult flare-up involving multiple joints. The drug is given intravenously each day over a period of six to eight hours, as the half-life of corticotropin is 1 to 17 minutes. This procedure should be followed by 0.5 mg. of colchicine twice daily for 10 to 14 days to prevent rebound attacks.

Acute Rheumatic Fever

The influence of the adrenal cortical steroids in rheumatic fever must be evaluated from two standpoints. One is the immediate effect on the signs and symptoms of the disease during the acute phase and the other is the influence on cardiac involvement when measured two or more years after the acute attack.

Many physicians who treat acute rheumatic fever prescribe large amounts to the patient as soon as the diagnosis is suspected or confirmed. The earlier it is given the greater the possibility it will be effective, certainly not later than three weeks after onset of the disease. There is usually prompt suppression of the clinical manifestations, i. e., arthritis, fever, and tachycardia. The drug should be given in generous amounts as long as this suppression is necessary. The dosage should be varied, depending on the activity of the rheumatic fever, and stopped altogether when the clinical manifestations have subsided.

The greater benefit has been observed in the patient's cardiac status several years after the acute episode. If such an attack is treated early and with adequate doses, the incidence of rheumatic heart disease is lessened. This is very encouraging, as it appears to be a milestone in the prevention of cardiac complications such as heart failure in later life. Here, again, it is necessary to emphasize the use of adrenal steroids early in the attack of acute rheumatic fever in order to derive the greatest benefits.

Rheumatoid Spondylitis

There are some patients who require the use of adrenal steroids in rheumatoid spondylitis from time to time. The general application is similar to the use of adrenal steroids in rheumatoid arthritis and will be discussed under that heading.

Osteoarthritis

Although osteoarthritis is not a rheumatoid disease, adrenal steroids, when used intra-articularly, may be effective in relieving pain and swelling. An injection, into the joint space or into the periarticular structures, of hydrocortisone (Cortef, Cortril, Hydrocortisone, Hydrocortone) acetate, prednisolone butylacetate (Hydeltra-T. B. A.) or methylprednisolone (Medrol) often produces prompt as well as lasting improvement. Any peripheral joint can be injected easily, including the proximal interphalangeal joints. Although the hip joint responds least well of all the joints, a sufficient number are benefited to warrant a trial. The patient who has one or two painful joints due to osteoarthritis should receive two or three intra-articular steroid injections. The time interval is determined by the relief of symptoms. In Hollander's[2] series of over 74,000 injections, complications were rare. The oral administration of adrenal steroids in osteoarthritis is of little or no value.

Collagen or Connective Tissues Diseases

Inasmuch as this group of disorders may have rheumatoid changes as part of the complete syndrome, it should be included in this report. In general, it is assumed that the administration of adrenal steroids is suppressive. Some physicians believe that life may be prolonged by steroids when given to patients affected with a mild or moderately severe collagen disorder. There is general agreement that, during acute episodes their use is definitely indicated and may be lifesaving. During this phase large doses should be given in order to control the clinical state of the patient. Also, if one steroid does not appear to be effective, others should be tried, as there may be a difference in response in certain patients. After the acute episode the dosage should be reduced to a minimum or eliminated altogether, if possible. Therefore, it is advisable to use adrenal steroids only at such times in the treatment of collagen or connective tissue diseases as the patient requires them for acute symptoms not controlled with other medication.

Professor and Head, Department of Therapeutics, University of Buffalo Medical School and Attending Physician, Buffalo General Hospital.

Rheumatoid Arthritis

The suppression of the signs and symptoms of rheumatoid arthritis after the administration of adrenal cortical steroids startled the medical profession. Incentive for research in arthritis, as well as in many other fields, followed. Physicians had renewed interest in arthritis, which led to improved medical care for the patient. As the result of 10 years' experience, the adrenal cortical steroids are not used routinely in the treatment of rheumatoid arthritis but only during certain phases of the disease, as listed later. Despite various schedules of dosage, the effect of these drugs is temporary. Within 48 hours after cessation of therapy, most patients revert to the previous arthritic state. There is no dose of these steroids low enough to produce clinical improvement without the development of side-effects in the patient. The usual complication is that of clinical hypercortisonism as evidenced by adrenal cortical hyperfunction (Cushing's syndrome), with one or more of the changes such as moon face, buffalo hump, hirsutism, striae, glycosuria, hypertension, and osteoporosis. These may occur in various degrees.

Most physicians are convinced that a basic program of management is the proper plan of therapy for the patient with rheumatoid arthritis. This includes a period of complete bed rest and physical therapy and analgesic medication administered with sincere, interested, medical attention. There is an increasing return to gold therapy as part of this program.[3] Adrenal steroids are not given routinely to the patient with mild or moderate joint involvement, as the course of the disease is frequently controlled with "conservative" treatment. Inasmuch as the adrenal steroids are only suppressive, the patients under their influence have a false sense of security. At that time they are apt to be too active physically, thus mechanically aggravating the underlying arthritis without warning to the patient. In addition, the ulcerogenic tendency (whether it refers to a new or reactivated ulcer) complicated by hemorrhage or perforation, along with masking of infections, purpuric manifestations, and production of adrenal inactivity or atrophy may be serious complications when adrenal steroids are given over a long period of time. However, there are several phases during the course of rheumatoid arthritis when adrenal cortical steroids should be used to the permanent benefit of the patient. They should be given a thorough trial under the folllowing conditions:

1. The patient with severe rheumatoid arthritis deserves a trial with adrenal steroids. Often great relief can be obtained with small amounts. The attending physician must visit the patient regularly to adjust the dose of the steroids, depending on the effectiveness of therapy. Often a patient who is in great pain and discomfort may experience marked prolonged improvement with minimal amounts. Even with small doses of steroids, however, it is expected that side-effects will appear sooner or later. In this group of patients, most of them will do very well as soon as a minimum dosage is established in relation to the side-effects the patient is willing to endure in order to obtain relief of symptoms.

2. Patients who, during the course of the disease, have severe constitutional signs of tachycardia, anemia, fever, and weight loss will need steroids in large amounts. They may save the lives of some patients. Often these exacerbations are of short term, perhaps several months, after which the steroids may be discontinued entirely. A higher percentage of those with juvenile rheumatoid arthritis will experience this type of exacerbation than those with the adult type. It is in these patients, also, that it may be necessary to shift from one steroid to another in order to obtain the maximum effect. The administration of steroids to these patients is mandatory.

3. During the course of gold therapy some patients develop dermatitis, which does not improve on cessation of the gold salt medication nor respond to other measures. Such patients will often derive great benefit when given an adrenal steroid to control the itching and irritation due to the dermatitis.

4. One of the greatest uses of adrenal steroids is in the group in which a program of rehabilitation has been planned. This is especially helpful when measures are used to attempt to extend completely a partially flexed joint, such as the knee, during the first time a cast is applied. Usually much time is saved, as greater range of motion is possible when the patient is receiving steroid medication. This should be administered intra-articularly as well as orally. The adrenal steroid is started one week before, and discontinued within two weeks after, application of the cast. Another phase of rehabilitation which is made easier by use of adrenal steroids is during the time that the patient is trying to learn exercises or to use apparatus such as the wheel or wands. Also, exercises for non-weight-bearing muscle are much easier to teach when the patient is receiving steroid therapy.

5. The intra-articular use of steroids is important; in many cases, the action appears to be more than suppressive, as excellent responses may persist for long periods. Range of motion is increased, swelling recedes, and pain is lessened. Steroids should be administered intra-articularly to the patient when one or two joints are more troublesome than the others. It is necessary to inject the drug into the joint space to obtain the best results. However, infiltration of the periarticular structures of the phalangeal joints or the elbow joint may also produce a favorable response. Reactions are unusual with this route of administration, provided strict surgical asepsis is followed. The most satisfactory improvement after injection of steroids occurs in the joints of fingers, elbows, and knees. The frequency of injections is governed by return of symptoms; they may be given weekly or at longer intervals. If there is no improvement after three weekly injections, this type of treatment should not be continued. Again, it must be emphasized that every effort must be made to inject the adrenal steroid intra-articularly in order to obtain the most relief.

Adrenal steroid therapy should not be used routinely during the initial treatment of rheumatoid arthritis, especially if the disease is mild or moderate in severity. Conservative measures should be used first. Steroid therapy should not be given along with gold salt therapy, as it tends to nullify the beneficial effects of the gold.

The physician assumes a great responsibility when he initiates the use of adrenal cortical steroids in a patient with rheumatoid arthritis. Generally, with the exceptions stated previously, the effect of these steroids is temporary, having little or no permanent benefit on disease structures in or around the affected joints. However, the patient does feel so much better for a varying period of time, extending for months, that continued use is most pleasant for the patient. However, there comes a time when the symptoms are not controlled, despite increased dosage, and, at that point, the patient becomes one of the most difficult problems in rheumatology. After weeks of attempts to discontinue administration of steroids, some patients are comfortable with gradual prolonged reduced dosage of the steroid to the point where no more is necessary and other analgesic medication is substituted. But many patients will never stop using steroids, and life becomes a more unpleasant problem than ever. It is in these patients that the most serious complications of adrenal cortical steroid therapy are most apt to occur. Therefore, in the patient with mild or moderate rheumatoid arthritis, it is highly desirable to outline a conservative program of management, including gold salt therapy, before any steroids are given.

Before concluding this discussion it is appropriate to describe some of the common reactions to prolonged administration of adrenal cortical steroids or corticotropin.

1. Cushing's syndrome of clinical hypercortisonism may develop, consisting of moon face, buffalo hump, hirsutism, striae, and edema. These signs usually disappear after discontinuance of the drug. However, glycosuria and hypertension, also part of this syndrome, may be permanent.

2. Negative nitrogen, calcium, or phosphorus balance may occur, with subsequent osteoporosis which may lead to bony

fractures. The concomitant use of anabolic hormones, especially in the postmenopausal woman, is desirable if prolonged administration of the steroids is necessary.

3. Gastrointestinal complications may develop into a serious disability. Peptic ulcers may develop or become reactivated, with complications such as bleeding and perforation. It is necessary to keep the contents of the stomach alkaline or at least neutral by the administration of antacid with each dose of steroid to prevent peptic ulcer formation.

4. Masking of infections is not uncommon. Fever or other complications such as perforation may not be detected. There is an interference with normal immune processes of the body, and unrecognized septic processes may develop rapidly or even result in death. The early use of antibiotics is necessary. Acute appendicitis, perforation of a peptic ulcer, or a diverticulum can occur—only to be recognized too late to save the life of the patient. Apparently the adrenal cortical steroids interfere with the normal mechanism of immunity, causing the unrecognized septic processes to occur.

5. Flushing of the face and purpuric spots in the skin are more common with the newer steroids. In some instances, these areas may be 3 to 4 cm. in diameter. The outer layer of the skin may rub off easily.

6. The production of adrenal inactivity or atrophy endangers the patient during periods of extra stress which may occur during fatigue, infections, or surgical procedures. The patient needs protection with the adrenal cortical steroid during stress for months after original therapy has been discontinued. In some patients it is necessary to use the adrenal cortical steroids parenterally.

7. There is the possibility of changing host-tissue responses so that the patient develops vascular angiitis, polyarteritis, or other collagen diseases. There is no positive proof at this time, but the evidence is strongly suggestive.

8. Patients with rheumatoid arthritis must be warned that excessive activity is to be avoided; otherwise the arthritis may worsen during the period of steroid therapy, as warnings of pain and swelling may be concealed for a time.

Summary

Ten years' experience is now available with the use of the adrenal steroids in the treatment of the rheumatoid diseases. During this period a variety of new adrenal steroid compounds have been developed, with the hope of making available for general use substances devoid of the potential for producing certain complications. To date, it has not been possible to accomplish this end. It has therefore become important to recognize the risks incurred with long-term use of the adrenal steroids as weighed against theoretical advantages. It would appear at the present time that these risks, in general, outweigh any advantages. Therefore, in the individual case, careful consideration is essential before beginning administration of adrenal steroids. The clinical situations in the field of rheumatic and collagen vascular diseases in which the long-term use of the adrenal steroids appears justified are actually few if indications are carefully appraised prior to their use.

References

1. Hench, P. S.; Kendall, E. C.; Slocumb, C. H.; and Polley, H. F.: Effect of Hormone of Adrenal Cortex (17-Hydroxy-11-Dehydrocorticosterone; Compound E) and of Pituitary Adrenocorticotropic Hormone on Rheumatoid Arthritis: Preliminary Report, Proc. Staff Meet., Mayo Clin. *24*:181-197 (April 13) 1949.

2. Intra-articular Use of Steroids, technical exhibits, Clinical Meeting of A. M. A., Minneapolis, Dec. 2-5, 1958.

3. Lockie, L. M.; Norcross, B. M.; and Riordan, D. J.: Gold in Treatment of Rheumatoid Arthritis, J. A. M. A. *167*:1204-1207 (July 5) 1958.

J.A.M.A. *170*:119/1063 (June 27) 1959.

REPORT TO THE COUNCIL

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known; its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN RHEUMATIC FEVER

Currier McEwen, M. D., New York

Any discussion of therapy in rheumatic fever must, of course, be concerned with the extremely important aspect of prevention as well as with treatment of the attack which has already begun. The measures of importance in prevention can be stated with confidence in the light of progress made over the past 30 years. Unfortunately, however, one can write with far less certainty about the treatment of the established attack. In this presentation, both prevention and treatment will be considered and the evidence for and against the important unsettled issues will be briefly discussed. In addition, some aspects of the treatment of patients with inactive rheumatic heart disease will be included.

Prevention

The evidence that rheumatic fever does not occur without a preceding infection due to a group A hemolytic streptococcus is now so well established that it is necessary to mention only a few of the more important recent studies in a discussion such as this. Indeed, as long as 20 years ago, almost everyone studying the disease had accepted the convincing evidence provided by the antistreptolysin-O determination, which had been repeatedly shown by Coburn and others to be high in some 85% of patients with rheumatic fever, irrespective of whether there had been a clinically apparent preceding hemolytic streptococcic infection. Nevertheless, there still were a few investigators who believed that some, at least, of the remaining 15% of cases might have other causes. Then, in 1954, Stollerman and co-workers showed that, if one used tests for not merely one but three hemolytic streptococcic antibodies, positive evidences of a recent infection by these micro-organisms could be demonstrated in approximately 99% of cases. Thus, the evidence is now overwhelming that a prior hemolytic streptococcic infection is an essential to all attacks of rheumatic fever.

The important practical application of these basic studies has been the demonstration that, by prevention of hemolytic streptococcic infections or by prompt, intensive treatment of an existing infection, rheumatic fever can, in turn, be prevented. Prevention thus can be considered under two headings, continuous prophylaxis against the start of a hemolytic streptococcic infection and intensive treatment of an infection which has begun.

From the Department of Medicine and the Rheumatic Diseases Study Group, New York University College of Medicine and the Third Medical Division, Bellevue Hospital Center.

Continuous Prophylaxis.—There are a number of satisfactory regimens for continuous prophylaxis. The ones which will be mentioned here are those recommended by the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association, listed in the order of my preference: (1) benzathine penicillin G (Bicillin, Permapen), one intramuscular injection of 1,200,000 units every four weeks; (2) sulfadiazine or a preparation of multiple sulfonamides in doses of 500 mg. (for children weighing under 60 lb. [27.2 kg.]) or 1.0 Gm. (for persons weighing 60 lb. or more) daily by mouth in a single dose; or (3) penicillin in the form of a buffered soluble salt of penicillin G, sodium penicillin O (Cer-O-Cillin sodium), or phenoxymethyl penicillin (Pen-Vee, V-Cillin), 250,000 units by mouth two times daily. All these regimens are effective, but benzathine penicillin G given intramuscularly has consistently been found to give slightly greater protection than the others. This probably is due, at least in part, to the special advantage that, since the physician gives the injection himself, he can be certain that the patient is really receiving it. All too frequently when oral medication is being taken at home, doses are missed sufficiently often to permit a hemolytic streptococcic infection to break through. However, in patients who object to an injection once each month or in the occasional patient in whom local reactions occur at the site of injection severe enough to make this method inadvisable, either of the other regimens will give excellent protection if followed faithfully by the patient.

There are two vital questions concerning continuous prophylaxis. Who should receive it, and how long should it be continued? Absolute answers cannot be given to either question at present, but the following rules are recommended. Continuous prophylaxis should be given to any child (and probably also to any patient below the age of 25 years) who has ever had an attack of rheumatic fever or who has definite heart disease of the rheumatic type, even in the absence of a history of any illness suggesting rheumatic fever. In adults, it should be given after a recent attack of rheumatic fever or if rheumatic heart disease (active or inactive) is present. It probably is not indicated merely because of a history of rheumatic fever in the remote past in an adult whose heart is normal.

The question of length of time prophylaxis should be continued is particularly difficult. In the present state of knowledge, it probably is best to start continuous therapy with the thought that it will be kept up throughout the patient's life if heart damage already exists, and at least well on into adulthood in a child with a history of rheumatic fever but with a normal heart. It can be hoped that, before many more years have passed, new information will be available which will permit a better answer to this question. Meanwhile, no rules of thumb can be established governing continuous prophylaxis which can supplant the judgment of the physician responsible for the individual patient.

Another point of importance in continuous prophylaxis is the need for higher doses given temporarily to provide added protection when procedures such as dental extractions and major or minor surgical operations are being performed which permit bacteria to enter the blood stream. Penicillin and sulfonamides in doses used for continuous prophylaxis are sufficient to prevent infections by hemolytic streptococci and other sensitive bacteria. The blood levels induced are not high enough, however, to control alpha hemolytic streptococci or other resistant micro-organisms. Hence, additional protection is indicated when there is danger that the introduction of bacteria may cause the implantation of bacterial endocarditis on heart valves already damaged by rheumatic valvulitis. The following regimen is recommended: On the day of operation, 600,000 units of an aqueous soluble penicillin G salt plus 600,000 units of procaine penicillin G (Crysticillin, Depo-Penicillin, Diurnal Penicillin, Lentopen, Procaine Penicillin G) are given by injection shortly before the operative procedure. For two days after, 500,000 units of penicillin are administered orally four times a day. For patients who cannot be given penicillin, erythromycin (Erythrocin, Erythromycin, Ilotycin) or the broad-spectrum antibiotics can be used. In patients who are to undergo surgery of the urinary or lower gastrointestinal tract, oxytetracycline (Terramycin) hydrochloride or chlortetracycline (Aureomycin) hydrochloride should be administered in full doses instead of penicillin. Similar protection should be given to patients with congenital heart disease who are to undergo any procedure likely to be associated with transient bacteremia.

Finally, it must be emphasized that the discovery of the value of continuous prophylaxis places a greater responsibility than ever on the physician for making a correct diagnosis of rheumatic fever and of rheumatic heart disease. Failure to institute protection when it is required will often result in further rheumatic attacks, with the tragic progression of cardiac damage so familiar before the era of continuous prophylaxis. On the other hand, it is no light matter to start a patient who does not need it on a course which calls for a continued administration of a drug over a period of many years. In this dilemma strict diagnostic criteria are advisable, such as the "modified Jones Criteria" obtainable through the American Heart Association. If the diagnosis is in doubt it probably is preferable not to start continuous prophylaxis but to warn the patient of the possible special hazard to him of hemolytic streptococcic infections. Then, at the first symptom of sore throat, a culture can be taken, and, if the infection proves to be due to hemolytic streptococci, intensive penicillin therapy can be given as outlined in the following section.

Penicillin Therapy.—Massel, Rammelkamp, and others have shown that intensive antibiotic therapy of a hemolytic streptococcic infection of the pharynx will prevent the subsequent development of rheumatic fever. The sooner this can be started the better, but there is good evidence that it is worth while even up to the 10th day after the start of the infection. Two points of major importance must be stressed. The first is that a bacterial agent is required for the elimination of an existing infection, whereas a merely bacteriostatic agent like sulfadiazine is effective in continuous prophylaxis to prevent a hemolytic streptococcic infection from starting. Hence, the sulfonamides cannot be used for this purpose. The second point is equally important, namely, that an effective blood level of penicillin must be maintained at least 10 days to eliminate all viable hemolytic streptococci. Shorter treatment may give a transiently negative throat culture, but, if the effective blood level is maintained less than 10 days, the cocci frequently reappear. Unless the streptococci are completely eliminated, rheumatic fever may occur.

For intensive therapy of an existing hemolytic streptococcic infection, the following regimens are recommended: (1) a single intramuscular injection of 600,000 to 900,000 units of benzathine penicillin G for children and 1,200,000 units for adults; (2) a buffered soluble salt of penicillin G, potassium penicillin O, or phenoxymethyl penicillin, 250,000 units by mouth two times daily for 10 days; or (3) procaine penicillin G with aluminum monostearate in oil, 300,000 units for children and 600,000 units for adults given intramuscularly every third day for three doses.

This form of prevention of rheumatic fever is so simple and direct that it is tempting to rely on it alone. Unfortunately, however, this cannot be done in a patient who has proved to be susceptible to rheumatic fever because of the well-known fact that, in close to 50% of attacks of rheumatic fever, the inciting hemolytic streptococcic throat infections are so mild that they may pass unnoticed. Hence, intensive therapy of throat infections is of value mainly as a "second line of defense" for the treatment of infections which may break through a carelessly followed regimen of continuous prophylaxis. Obviously, also, therapy is indicated in the treatment of any patient, with rheumatic disease or not, with a hemolytic streptococcic infection. Penicillin is used far too often for viral infections of the throat, in which it is ineffective. On the other hand, it is

all too frequently given for too short a time in true hemolytic streptococcic infections. There can be no doubt that many first attacks of rheumatic fever could be prevented if adequate blood levels of penicillin were always maintained for a full 10-day period in the treatment of streptococcic pharyngitis.

Treatment of an Established Attack

In contrast to the important advances which have been made in the prevention of rheumatic fever, the current status of treatment of an attack which has already begun is confused and unsatisfactory. Indeed, there are few, if any, measures today which can be claimed with certainty as better than those available 50 years ago. In the remainder of this section, consideration will be given to various time-honored measures of treatment and to the following unsettled questions. Are the corticosteroids (glucocorticoids) and salicylates of value in the treatment of carditis, and, if so, are the former superior to the latter? Should both be used together? Does penicillin have a curative as well as a prophylactic effect?

Time-Honored Measures.—Among the time-honored measures of treatment are salicylates, rest, and various measures for the treatment of heart failure.

Salicylates: The great value of salicylates in the treatment of the polyarthritis and fever of rheumatic fever remains unchallenged. Indeed, there probably is no therapeutic response in all of medicine more striking than that of rheumatic polyarthritis to these drugs. On the other hand, in spite of opinion to the contrary by some European physicians, it was almost universally believed in the United States and Great Britain up to relatively recently that salicylates had little or no effect on rheumatic carditis. This belief was based on the frequent appearance and progression of severe carditis while the patient was taking full therapeutic doses of salicylates, and also on the fact that rheumatic nodules could appear during salicylate therapy. Since these lesions are made up of microscopic granulomas like those of the myocardial Aschoff bodies, it was assumed that the granulomatous type of inflammation in the myocardium also progressed in spite of salicylates. During the past five years this opinion has been questioned in the United States as discussed later. Meanwhile, however, there never has been doubt as to the dramatic value of these drugs in polyarthritis. For maximal suppression of inflammation, a blood salicylate level of 25 to 35 mg. per 100 cc. of serum should be maintained, but polyarthritis and fever usually respond to smaller amounts. A dosage of 5 to 8 Gm. given daily in multiple doses of 1 Gm. each will suffice for the adult in most instances. Children require relatively less. Their dose may be computed on the basis of 60 mg. per pound of body weight daily for one or two days, then 40 mg. per pound daily for a week or 10 days, followed by 30 mg. per pound daily for as long as symptoms persist.

Digitalis and Diuretics: In the presence of congestive heart failure, digitalis and diuretics are indicated as in any other type of heart disease. Greater caution must be taken in digitalization than in congestive failure due to other causes, however, because rheumatic myocarditis appears to make the heart more than normally susceptible to the development of toxic arrhythmias.

Rest: In the absence of any effective treatment for carditis, complete rest in bed has long been the measure principally relied on. Up to 15 to 20 years ago, very strict rules governing rest were insisted on in the United States, as they still are in a few centers, namely, that, before rheumatic patients are allowed to sit up, they must have a temperature, sleeping pulse rate, and laboratory indexes of inflammation which are completely normal without salicylates for at least 10 days, as well as absence of all manifestations of rheumatic fever. During recent years, however, more and more American investigators tend to adopt a far less strict policy regarding rest. This has come about for three principal reasons: 1. There has been a growing realization that complete bed rest is more apparent than real, especially in children, once the acute phase of disease is past. 2. Various studies have suggested that allowing the patient to sit up does not do harm and may even be helpful. 3. In any event, the psychological damage caused by insistence on bed rest over periods of months probably outweighs any questionable physical benefit. In order to obtain a sample of current opinion regarding rest, 22 leaders in the field of rheumatic fever in the United States and Canada recently were queried with the following results: 6 of them still insist on strict bed rest for any patient with rheumatic fever, whether or not carditis is evident; 2 have adopted a moderately liberalized interpretation of the rules, even when carditis is present; and 14 allow the patient to start sitting up for short periods and to be taken to the bathroom once or twice each day as soon as acute pain, congestive heart failure, pericarditis, and gross tachycardia have subsided.

Value of Corticosteroids and Salicylates in Carditis.—With the advent of cortisone (Cortisone, Cortogen, Cortone), hope was high that at last an agent was available which would suppress rheumatic inflammation not only in the joints but also in the heart. However, nine years after the introduction of corticosteroid therapy in rheumatic fever it still cannot be stated with absolute finality whether these agents are of value in carditis or, indeed, whether they may not actually be harmful. Despite reports of favorable results by many physicians, including the author, in preventing serious heart damage from rheumatic fever, only one controlled study which meets statistical standards has been made. This was the "Cooperative Clinical Trial of ACTH, Cortisone and Aspirin in the Treatment of Acute Rheumatic Fever in Children," carried out by the Rheumatic Fever Working Party of the Medical Research Council of Great Britain and the Sub-committee of Principal Investigators of the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association. This careful study, based on 497 children with acute rheumatic fever treated at 12 centers in the United States, Great Britain, and Canada, failed to reveal any superiority of cortisone or corticotropin (ACTH, Acthar, Corticotropin) over aspirin, in terms either of the response of the acute disease or of heart damage after one year of follow-up.

In that study cortisone was given in total daily doses of 300 mg. for the first day, 200 mg. for the next four days, 100 mg. for the remainder of the first three weeks, 75 mg. for the fourth and fifth weeks, and 50 mg. for the sixth week. Because of the possibility that the corticosteroid dosage had been too low in the "Cooperative Clinical Trial," investigators from several of the participating centers joined with others in a similar clinical trial in which prednisone (Deltasone, Deltra, Meticorten, Paracort) was given in doses three to four times the equivalent of the previous therapeutic doses of cortisone for a period twice as long. Only children with clinically definite carditis in their first attacks of rheumatic fever in whom treatment could be started within the first three weeks of illness were included in the study. The actual daily dosage schedule of prednisone used was 60 mg. for the first three weeks, 50 mg. for the fourth week, 40 mg. for the fifth week, 30 mg. for the sixth week, and then gradual tapering over the next six weeks, so that the total amount given during the 12-week period was 3 Gm. The results in 24 children who received prednisone and 23 who received aspirin gave no support to the view that corticosteroids in large doses over a three-month period have any greater effectiveness than do salicylates in reducing the incidence of residual cardiac damage at the end of one year of follow-up. Furthermore, the "rebounds" of transient signs of increased disease activity so frequently seen after shorter courses of corticosteroids in rheumatic fever were also apparent after the longer courses. No serious untoward effects were noted. However, in view of the lack of evidence of ultimate benefit and the acknowl-

edged hazard of such large doses of corticosteroid, the group of investigators recently decided that continuation of the study was unjustifiable, and it has been stopped.

It was mentioned earlier that, after many decades of serious doubt in this country as to the value of salicylates in rheumatic carditis, there has recently been a trend toward a more optimistic attitude on the subject. Paradoxically, this has stemmed partly from the "Cooperative Clinical Trial of ACTH, Cortisone and Aspirin." When that study was designed, the group treated with aspirin was included to serve essentially as "untreated" controls from the standpoint of carditis. When close observation of the large number of patients studied showed that those treated with salicylates fared essentially the same as those receiving corticosteroids, the report concluded that "there was no evidence that any of the three agents resulted in uniform termination of the disease and on all treatments some patients developed fresh manifestations during treatment," and that "at the end of one year there was no significant difference between the three treatment groups in the status of heart." Nevertheless, in spite of this careful statement, it has frequently been assumed that the similarities in results in each treatment group meant that each treatment was helpful in lessening cardiac damage. Obviously, it might be concluded with equal reason that none of the treatments was effective. Since no completely untreated group was included, the study did not answer that question.

Assessment of the possible benefits that may be expected from corticosteroid or salicylate therapy in the various manifestations of rheumatic fever can perhaps be made clearer through consideration of the various phases of the disease process. These may be somewhat arbitrarily thought of under six headings: (1) the underlying mechanism of disease, (2) tissue injury, (3) the phase of acute exudative inflammation, (4) the phase of granulomatous inflammation, (5) the formation of scar tissue, and (6) the inactive phase of mature scarring. Considering these individually, there is no evidence that corticosteroids or salicylates affect either the underlying mechanism of disease or the stage of mature scarring. On the other hand, there is good evidence that both these agents strongly suppress the acute exudative inflammatory process. The evidence regarding suppression of tissue damage and of the granulomatous type of inflammation unfortunately is uncertain and conflicting. The subcutaneous rheumatic nodule can be cited as an example of a granulomatous lesion which can be seen and measured, yet reports as to the effect of corticosteroids on its evolution and disappearance are widely conflicting. A number of authors have reported the rapid disappearance of these nodules under the influence of cortisone and corticotropin, whereas others have noted no effect. In the "Cooperative Clinical Trial," new subcutaneous nodules appeared with approximately equal frequency during therapy with corticotropin, cortisone, and aspirin. In view of the conflicting conclusions regarding such easily observable lesions as subcutaneous nodules, it is not surprising that divergent results have been reported regarding the effects of corticosteroids on rheumatic carditis. Clearly, however, analysis reveals no unquestionable evidence of striking superiority of corticosteroids over salicylates, as judged by the ultimate development of organic valvular lesions. There remains the question of possible benefit which might be given by the proved capacity of corticosteroids to inhibit scar formation. That experimental effect in animals has been obtained, however, with far larger doses of corticosteroids than are used therapeutically. Again it must be concluded that the end-results of controlled studies do not suggest any greater prevention of valvular scarring by cortisone than by salicylates.

Summarizing this discussion of the possible effects of corticosteroids and salicylates on the various phases of rheumatic lesions, it would appear probable that only acute exudative inflammation is strikingly benefited. Thus, the value of these agents in the treatment of various manifestations of rheumatic fever probably depends largely on the severity of acute exudative inflammation. In rheumatic polyarthritis, in which this is the predominant feature and granulomatous lesions and scarring are minimal, corticosteroids and salicylates are extremely effective. In contrast, the acute exudative phase of inflammation probably is transient and of secondary importance in most instances of rheumatic valvulitis and myocarditis. Nevertheless, it is reasonable to hope that there may be some benefit in most patients with carditis if treatment can be started within the first few weeks of illness. In some patients with high fever and, especially, with severe pericarditis, agents capable of suppressing acute inflammation may be of great value.

Corticosteroids and Salicylates Used Simultaneously.—In view of the similar anti-inflammatory effects of corticosteroids and salicylates, many investigations have been carried out to test the possibility that the latter may act through stimulation of the pituitary-adrenal axis. From the standpoint of the treatment of rheumatic fever, the question is a practical one because, if salicylates act by stimulating an increased endogenous output of corticosteroids, there would be little reason to give the two together. On the other hand, if these agents act through different mechanisms, their simultaneous use in the same patient is reasonable. An abundant literature has already accumulated on the subject, with conflicting results and conclusions which it is unnecessary to review here. One may say in summary that the evidence does not support the view that the antirheumatic effect of salicylates is mediated through the adrenal cortex. It is, therefore, reasonable to use both agents together.

Intensive Penicillin Therapy.—Before discussing intensive penicillin therapy for rheumatic fever, it will be helpful to review very briefly the current views as to the possible mechanisms by which hemolytic streptococcic infections cause rheumatic fever. Four theories may be mentioned. According to one, the underlying mechanism is that of delayed hypersensitivity to streptococci or their products. According to the second, the disease results from autoantibodies to the patient's own tissue proteins which have been altered by streptococcic action. A third theory invokes the action, either direct or through the mechanism of delayed hypersensitivity, of a hypothetical specific toxin or enzyme common to "rheumatogenic" hemolytic streptococci. According to the fourth theory, the acute manifestations of rheumatic fever may have one of the aforementioned explanations, but the ultimate cardiac damage results from the persistence of living hemolytic streptococci, either as such or as "L" forms, which have invaded the heart muscle and valves.

The use of corticosteroids as outlined in the preceding sections is based on the hope of suppressing sterile inflammatory reactions resulting from such mechanisms as those underlying the first three theories. If, however, the fourth theory is correct, corticosteroids might be expected to be harmful because of their capacity to enhance the spread of infections. Therefore, intensive therapy with penicillin would be the logical attack.

Several studies carried out soon after the advent of penicillin indicated that, whereas this antibiotic was effective in preventing hemolytic streptococcic infections (and, hence, rheumatic fever), if taken daily throughout the year it did not benefit the acute manifestations of rheumatic fever if given after that disease had started. For some years the influence of these reports retarded any widespread use of penicillin in treating rheumatic fever until Massell's and Rammelkamp's demonstrations, previously referred to, that intensive use of a bactericidal agent like penicillin early in tonsillitis could prevent an ensuing rheumatic attack. After this there was gradual acceptance of the view that a similar intensive course of penicillin should be given early in rheumatic fever, with the aim of eliminating any hemolytic streptococci which the patient might still be harboring and which might tend to maintain rheumatic activity. During recent years this has become standard practice in the United States and in Great Britain. No experimental trial was made to test the value of such a regimen, however,

until the studies reported in 1959 by Mortimer, Vaisman, Rammelkamp, and their collaborators. These investigators carried the concept a step further by giving a more intensive course of penicillin than that previously used. This procedure was designed to eliminate not only streptococci in the throat but also any which (according to theory number four) might have lodged in the cardiac tissues where, hypothetically, they might be more difficult to eradicate. These investigators have reported on a preliminary study of 85 patients in Santiago, Chile and have considered the results to be sufficiently promising to warrant further evaluation.

The regimen of penicillin used was the following: 500,000 units of sodium penicillin G intramuscularly every four hours for 10 days, followed by procaine penicillin G intramuscularly twice daily for 11 days, then 1,200,000 units of benzathine penicillin G intramuscularly on the 22nd and 43rd days, and thereafter at five-week intervals. These patients also received aspirin in doses of 75 mg. per kilogram of body weight daily for 14 days. No differences were noted in 42 patients treated in this way compared with 43 patients given the aspirin alone, so far as the effect on the acute manifestations of rheumatic fever was concerned. Furthermore, subcutaneous nodules, pericarditis, and heart failure were at least as frequent during therapy in the penicillin-treated patients as in those receiving only aspirin. On the other hand, one year later the former group showed a "statistically significant" lesser amount of organic heart disease than did the latter.

Obviously this study needs confirmation before its real significance can be known, for the regimen of penicillin employed may offer no advantages over those currently in general use. It has been pointed out that a basic part of the treatment of rheumatic fever in recent years has been prompt institution of penicillin in doses large enough to eradicate hemolytic streptococcic from the throat. For this purpose, various treatment schedules have been used as outlined in the section on Penicillin Therapy. It has been assumed that, if the recommended doses are maintained for a minimum of 10 days, all viable hemolytic streptococci are eliminated in the great majority of patients because throat cultures subsequently are negative, and rheumatic attacks are prevented. Nevertheless, it may be that still more intensive therapy, approaching that used in the Santiago studies, is preferable in the case of the rheumatic attack which has already begun. Furthermore, if theory number four is correct and ultimate cardiac valvular damage in rheumatic fever does result from hemolytic streptococci harbored in the cardiac tissues, corticosteroid therapy could be expected to enhance their spread. Hence, on the grounds that are at present purely theoretical, it may be desirable to give penicillin fairly intensively throughout the period of corticosteroid administration.

Treatment of Other Manifestations of Rheumatic Fever.— In addition to fever, polyarthritis, and carditis, other less frequent manifestations of rheumatic fever include subcutaneous nodules, erythema marginatum, chorea, and pleurisy. The doubtful effect of corticosteroids and salicylates on subcutaneous nodules has already been discussed. It is generally agreed that these agents are without effect on erythema marginatum. Despite some reports of control of chorea minor (Sydenham's chorea) by moderate or massive doses of corticosteroids, most investigators believe that they are not effective and rely on rest and sedatives. Since inflammation of the acute exudative type often is a major component of rheumatic pleurisy, it is not surprising that this manifestation often appears to be benefited by corticosteroids and probably also by salicylates.

Patients with inactive rheumatic heart disease without heart failure, grossly abnormal cardiac rhythms, marked cardiac enlargement, or dynamically severe valvular lesions should not have their physical activities limited and should lead essentially normal lives. They should, however, be maintained on continuous prophylaxis against hemolytic streptococcic infections by one of the outlined regimens.

In the event of heart failure or important arrhythmias, appropriate measures should be instituted as is done for those manifestations in any other type of heart disease. Moreover, because of the possibility that such manifestations may indicate a fresh bout of rheumatic activity, evidence of the latter should be looked for, and, if found, intensive penicillin therapy should be given to eliminate any possible hemolytic streptococci which may be present.

Summary

Whereas the essential role of group A hemolytic streptococcic infections in causing rheumatic fever is now definitely established, the exact mechanism by which these infections cause the disease is not yet known. Advances of the utmost importance have been made in the prevention of rheumatic fever, including continuous prophylaxis for many years, designed to prevent the inciting hemolytic streptococcic infections, and intensive, early penicillin therapy of any hemolytic streptococcic infection which may occur.

In contrast to prevention, few advances of definitely proved value have been made in the treatment of the rheumatic attack which has already begun. Certain conclusions can be drawn, however, as follows.

1. The early hope that corticosteroid therapy could control rheumatic carditis and prevent lasting cardiac damage has not been borne out, and experience indicates that large doses given for long periods are hazardous and probably do more harm than good. It can be stated with considerable assurance that corticosteroids do not control the underlying, unknown mechanism of the disease and do not prevent the progression of permanent valvular damage. They have great capacity to suppress rheumatic polyarthritis and fever, but the same effects can be achieved with equal rapidity and greater safety by means of salicylates. It is possible that corticosteroids may be of value early in carditis through suppression of the acute phase of inflammation, although it has not been proved that they are more effective even for this than are full doses of salicylates.

2. Since group A hemolytic streptococci have been proved to incite rheumatic fever, it appears logical and important to eliminate early in the course of rheumatic fever any hemolytic streptococci that may be present, even though throat cultures may be negative. It is equally important to prevent any new infections by these micro-organisms.

On the basis of these principles the following regimens are suggested for the therapy of rheumatic fever.

1. Prompt and intensive therapy with penicillin should be instituted to eliminate any hemolytic streptococci which the patient may be carrying. For this purpose, any of the regimens outlined in the section on Penicillin Therapy probably is sufficient. However, in view of the theoretical possibility that hemolytic streptococci in the heart may be a factor which leads to ultimate valvular damage, and on the hypothetical assumption that they may be more difficult to eradicate there than in the pharynx, it may be preferable to administer larger doses than those recommended for the treatment of streptococcic infections of the throat. It must be emphasized, however, that there are as yet no data to indicate that, at the outset of the rheumatic attack, larger doses of penicillin are superior to those which have been recommended for the intensive treatment of a hemolytic streptococcic throat infection. It may be advantageous also to continue throughout the period of corticosteroid administration somewhat larger doses than are usually given for continuous prophylaxis, but current information does not warrant including this as one of the essential recommendations. For the latter purpose, 1,200,000 units of benzathine penicillin G could be given intramuscularly every two weeks rather than every four weeks as long as corticosteroids are being administered.

2. If carditis is not evident, it is suggested that salicylates be used without corticosteroids, in the doses which have been outlined.

3. If carditis is present and treatment can be started within the first 3 weeks of onset, most investigators believe corticosteroids should be given. For this purpose, prednisone (or other corticosteroids in equivalent amounts) may be given in doses of 10 mg. four times daily by mouth for 10 days. Thereafter the total daily dose may be reduced at the rate of 2.5 mg. daily until discontinued. Again, on rather empirical grounds, it is suggested that aspirin be given with the corticosteroid at the rate of 900 mg. five or six times daily for adults and on the basis of body weight for children, as described. The salicylate should be continued after corticosteroid has been stopped, as long as symptoms, fever, and erythrocyte sedimentation and C-reactive protein tests (or other tests for acute phase reactants) suggest continuing disease activity. The evidence for the value of corticosteroids even early in carditis is questionable. If they cannot be begun within the first three weeks of onset of the carditis or of a new exacerbation, this form of therapy probably is not warranted.

4. Although complete bed rest is necessary during the period of acute symptoms, most American investigators believe that, once this stage is past, the patient may be allowed to sit up each day, whether or not carditis is present. If carditis is not present, gradually increased walking can then be allowed. In attacks associated with carditis, however, walking probably should not be permitted until convalescence is well advanced.

5. Continuous prophylaxis begun during the acute illness should then be maintained; one of the regimens outlined should be followed, with the intention of keeping it up indefinitely.

Patients with inactive rheumatic heart disease and without cardiac insufficiency or grossly abnormal rhythms should not have their physical activities limited but should be on a regimen of continuous prophylaxis. Heart failure and arrhythmias call for the same measures as in other types of heart disease; in addition, it is recommended that, at their appearance, the patient be given a course of intensive penicillin therapy on the chance that they indicate a breakthrough of hemolytic streptococci and a new attack of low-grade carditis.

It must be emphasized that, whereas the regimens for prevention of rheumatic fever can be recommended with assurance, most of those for treatment of the rheumatic attack are unproved and are presented as reasonable measures in the light of what is known and what is not known about rheumatic fever today.

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REPORT TO THE COUNCIL

The Council has authorized publication of the following paper, which was presented as part of a symposium-panel discussion held in Washington, D. C., Sept. 25, 1958, on the Use and Abuse of Adrenal Steroids. This is the third paper in the series, the first and second of which appeared in THE JOURNAL *on June 20, and 27, 1959, pp. 951 and 1063.*

H. D. KAUTZ, M.D., *Secretary*

STEROID THERAPY IN SYSTEMIC INFECTIONS

MONROE J. ROMANSKY, M.D., Washington, D. C.

We are all familiar with the tendency of the adrenal cortical steroids to alter manifestations of a variety of clinical disorders, and, of course, these include infectious diseases. This was studied and strikingly demonstrated by Finland and coworkers[1] when the adrenal cortical steroids were given to carefully selected patients with lobar and viral pneumonias. These observations made it clear that the steroids could induce, in patients with pneumonia, striking defervescence and symptomatic relief, with a decrease or disappearance of not only the subjective signs but also the objective findings. These remarkable changes occurred despite the persistence of pneumococci in the sputum, the presence of bacteremia, and, in one instance, the spread of pneumonia to other lobes with subsequent development of empyema. The symptomatic changes apparently were independent of gross changes in the antibody response and were not accompanied by reversal of metabolic patterns consistent and characteristic of pneumonia and other severe trauma. Subsequent to the initial reports, many clinical and laboratory data have accumulated,[2] which attempt to answer some of these observations. There are several broad questions which as yet have not been answered. Are steroids really valuable in infectious diseases or useful in any particular area of infectious diseases? Since these agents may not be helpful, but may be harmful, can one be specific in their use, so that the advantages may be obtained without serious consequences?

Professor of Medicine, George Washington University School of Medicine.

Early in the study of these problems,[3] these agents, without antibiotics, were used in a variety of infections such as tuberculosis, typhoid, bacterial pneumonia, and bacterial endocarditis. Certain objective information was obtained from these studies. Steroid therapy used in these patients with acute febrile illnesses brought about rapid remission and reversal of the distressing clinical evidences of the illness. When the etiological agent could be demonstrated, as in bacterial pneumonia, typhoid, and subacute bacterial endocarditis, despite the remission of the clinical syndrome, there was frequently noted evidence of increased multiplication or spread of the micro-organisms.

The ability to detect the depression of immunity is difficult, and many of the disease syndromes for which patients are treated with steroids are the type in which the mortality is low and complications are infrequent. However, in certain areas, controlled studies have been helpful. For example, in infectious hepatitis, the use of steroids leads to rapid symptomatic improvement and a rapid fall in level of serum bilirubin. However, it has been shown that relapse occurred in 20% of the treated patients and did not appear in controls.[4] The hormone should not be employed in the average case but only for patients who are quite ill, especially those with marked anorexia.[5]

The effects of steroids were observed in a controlled study on the course of poliomyelitis,[6] as well as in acute streptococcic disease,[7] and indicated no particular effect on the acute disease or on the sequelae. There were no adverse or favorable effects.

The effect of steroids in mumps orchitis is controversial. There have been reports of rapid remission subsequent to their administration; on the other hand, controlled studies have indicated no difference in response to corticotropin (ACTH, Acthar, Corticotropin, Cortrophin) or a placebo.[8] However, in these controlled studies the doses were not very large.

The occurrence of infections as aggravations of preexisting ones or spontaneously in patients receiving steroids during treatment for other conditions is well known.[9] This occurrence has been a major factor in complete or partial cessation of therapy with these agents. We should be aware of the need for judicious observation before administering the steroids, particularly in patients in whom pulmonary tuberculosis might be present.

The degree of hazard of infection in patients receiving corticosteroids is not easy to evaluate. These agents may so camouflage the appearance of septicemia that the infection may only be noted at autopsy. There have been instances in which steroids were used in patients with fever of unknown origin, with the assumption that an infection rather than tuberculosis was present, only to have rapid progress of active tuberculosis, indicating that this diagnosis had been missed. The danger to a particular patient receiving steroids may also vary according to his basic status. Intercurrent infection is more likely to develop in persons with a debilitating type of illness who receive steroids than in those with a milder illness or with a chronic illness such as rheumatic fever, in which debilitation is not a prominent factor.

Examples of the hazard of infection in patients receiving steroids are the 12 fatal cases of chickenpox in children reported by Haggerty and Eley.[10] The children were receiving steroids at the time of exposure to the disease.

From the experimental side it has been demonstrated that large doses of steroids definitely depress resistance to infections. This has been documented with experimental studies with bacterial, viral, fungal, protozoan, and even helminthic agents.[3b]

One would anticipate from the aforementioned statements that chemotherapeutic agents would counteract the adverse effect of the steroids. On the other hand, as shown in experimental animals, increasing the dose of steroids may overcome the effect of a given dose of a specific protective chemotherapeutic agent. This relationship is also limited by the toxicity of the particular substances. An example is the protective ability of penicillin in pneumococcic or group A beta hemolytic streptococcic infections in which this protection is diminished by the simultaneous administration of cortisone (Cortisone, Cortogen, Cortone). The effect of cortisone is overcome by increasing the dose of penicillin. However, it does not necessarily follow if tetracycline (Achromycin, Panmycin, Polycycline, Tetracyn, Tetracyn V) or chloramphenicol (Chloromycetin) is used instead of penicillin,[11] since the broad-spectrum agents are bacteriostatic generally and not bactericidal and the toxicity of these agents limits the increase in dosage.

Host resistance obviously also plays a role in determining the relative response to steroids and antibacterial agents. As shown by Johnson and Davey,[3a] relatively small amounts of streptomycin will overcome the effects of cortisone on tuberculosis in rats or rabbits in whom native resistance is relatively high; however, even with large doses of streptomycin, it is difficult to overcome all the adverse effects of cortisone on tuberculosis in guinea pigs. In essence then, the ability of specific agents to overcome the adverse effects of steroids in infection is a function of the host resistance and the virulence of the organism, as well as general characteristics of the drug.

Evaluation of clinical data on the relative effects of steroids and antibacterial agents is consistent with the points just made. The simultaneous administration of penicillin and cortisone to patients with pneumococcic pneumonia produced defervescence and symptomatic improvement more promptly than in those given penicillin alone. This was a carefully controlled study.[12] No adverse bacteriological results occurred, but renal insufficiency and prolonged hypothermia occurred in one patient treated with cortisone. Hypothermia has been reported by others[13] as a complication of cortisone therapy. This represents a situation in which the amount of penicillin used is adequate to overcome any possible reduction in host resistance induced by cortisone. We currently have a controlled study under way, comparing tetracycline and steroids.

Data have not been so favorable when infections have been studied in which specific treatment is more difficult. For example, in typhoid and brucellosis,[14] rapid defervescence follows the combined use of steroids and chemotherapy. However, no carefully controlled studies are available as there are with pneumococcic pneumonia, and one cannot be sure whether the improved response may not conceal an increased hazard. In a small series of patients acutely ill with brucellosis, prompt improvement occurred when cortisone was given for three or four days.[15] Apparently it was not harmful. Dubious results had been seen in patients with the more chronic stages of the disease.

A careful attitude was assumed early in the use of steroids in the management of patients with active tuberculosis. It was demonstrated experimentally that steroids suppress inflammation in the tissues but that tubercle bacilli multiply more rapidly. It is interesting, however, that there have been reported so few persons with spread of the disease while receiving steroids. Steroids do have a place in select cases of tuberculosis in conjuction with adequate chemotherapy. This seems to be particularly so in the more acute cases, as demonstrated by Johnson and colleagues[16] in a well-controlled study. They showed the rapidity with which patients with tuberculous meningitis improved and how promptly the abnormality of the spinal fluid could be corrected with the use of steroids. It has been suggested that the maximum period of therapy with steroids should be approximately three weeks. In this study, it was felt that the clearing of the fluid reflected the speed with which the exudative features of the disease could be reversed by steroids. It is well to bear in mind, however, that the number of controlled observations are few, and a rather marked improvement in management of tuberculosis in recent years makes it necessary to evaluate carefully whether the steroids have really contributed to the ultimate outcome.

Substantial symptomatic relief will usually occur when steroids are used with effective antibiotics. However, many infections, particularly those due to staphylococci and certain gram-negative bacteria, are difficult to manage with available agents. It is conceivable that the steroids in these situations may produce a more pronounced adverse effect because the agents are not as effective. These problems are under study, and currently no adequate clinical material is available for analysis. One is impressed by this need, despite claims for effectiveness of combined steroid-antibiotic therapy. Difficulties in evaluation have been noted by Lepper and Spies,[17] who studied these agents over a six-year period in over 1,000 persons. Although such agents are difficult to evaluate, they could not ascribe any marked benefits.

Antibacterial agents have been used as a prophylactic measure in patients receiving steroids. This is indeed a complex problem. Chemoprophylaxis generally has been effective when it has been used to eliminate susceptible micro-organisms such as group A beta hemolytic streptococci or meningococci, but it has not been particularly so when dealing with staphylococci or with gram-negative bacteria, particularly those which readily become drug-resistant. Prophylactic regimens will hardly be expected to confer adequate protection.

With the common antibiotic-resistant organisms, the feeling of security that the clinician may have in supposedly protecting the patient by chemoprophylaxis is hardly justified. It is particularly important that, when prophylactic chemotherapy is used, the dose of the agent is an adequate therapeutic one.

Available evidence strongly suggests that steroids, when given in sufficiently large amounts, do depress resistance to

infections and that ability of antibiotic agents to overcome the disease despite the depressed resistance is limited. When the limitations are not in effect, the chemotherapeutic agents frequently do overcome the disease despite the depressed bodily resistance.

The experimental data may help us in understanding the use of steroids. The value of steroid hormones in adrenal insufficiency is well established. Studies by Finland and colleagues[2b] illustrate the response of the infected adrenalectomized mouse to cortisone. An uninfected adrenalectomized mouse was maintained well with 5 to 10 mcg. of cortisone daily. A dose of specific antiserum was selected which protected 50% of the nonadrenalectomized mice against approximately 50,000 virulent pneumococci. The same dose of antiserum protected 50% of the adrenalectomized mice against only about 1,000 pneumococci. With the administration of 25 mcg. of cortisone per day, resistance returned to nearly that of the intact animals. Doses of 25 to 100 mcg. of cortisone were almost optimal, but larger doses, such as 500 mcg., depressed resistance to a degree comparable to that produced by adrenalectomy. Thus, it would appear that infection places greater demand for steroids on the host. In addition, the optimal dose of steroid is critical, and an excess is likely to be harmful. Objective means for determining the optimal dose clinically are not yet available.

The evidence is questionable that adrenal insufficiency occurs as a consequence of severe sepsis, in the absence of preexisting adrenal cortical hypofunction (Addison's disease). Although direct effects of bacteria or the endotoxins on the adrenal cortex may lead to adrenal insufficiency, pretreatment with cortisone protects the adrenals from the damaging effects of, for example, diphtheria toxins but does not protect the animal from the lethal action of the toxin. It would appear that the damage caused by the toxin is so widespread that protection of the adrenal gland alone is of little benefit to the host. Recently it has been shown that endotoxins from gram-negative bacteria inhibit steroid genesis in the perfused adrenal gland.[18] Large amounts of endotoxin were used in this experiment, that is, large by in vivo standards. The possibility of direct damage to the adrenal as a cause of adrenal insufficiency cannot be discounted, despite the fact that the circulating corticosteroid levels in the animals given lethal doses of endotoxin were generally above the normal range.[19]

Of the clinical syndromes considered to be associated with adrenal insufficiency, none is more so than meningococcic toxemia with collapse, in which the use of steroid and related compounds is generally recommended as part of therapy. Controlled observations of the value of adrenal steroids in this situation are difficult to find. Since the introduction of steroids, a variety of them have been used, with varying degrees of enthusiasm. Although there is general agreement that the steroids should be given to patients with shock, there is apparently no definitive satisfactory evidence that a favorable response can be ascribed to the adrenal hormones. Failures have occurred after the use of such steroids,[17] and the collapse in this infection has been successfully corrected by treatment with levarterenol (Levophed), without corticosteroids.[20] Some authors emphasize the need for a pressor agent such as levarterenol to be administered along with the adrenal hormones and chemotherapy.[21] It is quite apparent that more information is needed concerning the value of the steroids in the management of meningococcic infection with shock.

All of us are aware that adrenal insufficiency may occur if infection appears in patients in whom exogenous steroids have suppressed steroids genesis. Under such circumstances, there is justification for increasing the dose of steroids. On the other hand, in patients who have received the steroids for a time but whose conditions have begun to deteriorate, this deterioration may be due to unrecognized infections. Increasing the dose of such agents under these circumstances is likely to aggravate the infection, unless specific chemotherapy is begun. The amount of steroid to be given to patients with relative adrenal insufficiency is still determined empirically. This is so, since determination of the level of circulating steroid in any instance may not necessarily reflect the rate of production or turnover in the host. Detailed study is required to answer this question. Adrenal insufficiency apparently may be a rare complication of severe sepsis. Relatively little objective support exists for the concept that adrenal insufficiency is common in severe infections and that the use of steroids is justified on that basis.

It has already been noted that the steroid levels are usually elevated in patients during severe infections. It is possible that, under certain circumstances, small doses of exogenous hormone might conceivably cause more steroid to enter tissue cells.

The protective effect of steroids against bacterial endotoxin depends on increased blood levels of steroids at the time of contact between endotoxin and susceptible tissues.[22] The protective action of cortisone is not demonstrable in toxemias due to exotoxins from Corynebacterium diphtheriae, Clostridium tetani, Cl. botulinum, Cl. perfringens, or Shigella dysenteriae.[2b]

Adrenal corticosteroids are effective in diminishing the inflammatory response, regardless of the stimulus. Dougherty[23] has analyzed the various stages of the inflammatory response in an attempt to determine at which level the corticosteroids influence the process. Existing evidence indicates that the primary focus of steroid action is on vascular responsivity. In general, the effects of steroids on inflammation and repair can be explained on the basis of their effect on vascular tone and permeability. The effects of corticosteroids on hypersensitivity reactions and similar tissue responses to immunologically active stimuli probably reflect the general anti-inflammatory effect of these steroids rather than a specific effect on purely immunological mechanisms.

At present, it is generally agreed that steroids depress antibody production but do not alter the degradation rate of the preformed antibodies.[24] The mechanism by which this happens is not quite clear. There may be several ways in which this occurs. For example, the antigen may be held locally, due to a vascular effect of the steroids. The antibody-forming mechanism may be directly depressed, or the relationship with the antibody-forming cells to the intermediary cells in the process of antibody production may be altered.

As far as the steroids and particularly the reticuloendothelial function are concerned, from available evidence, it would seem that this function is disturbed by administration of the steroids and that this disturbance is manifested less in the initial response of the reticular cells to an injected load than in the capacity of these cells to recover their function after such a load has been administered.[25]

In conclusion, it is quite obvious that the exact status of steroids in the collateral management of infections is still not definitive and requires much in the way of further controlled clinical study.

References

1. Finland, M.; Kass, E. H.; and Ingbar, S. H.: Effects of ACTH in Primary Atypical (Viral) Pneumonia and in Pneumococcal Pneumonia, in Proceedings of the First Clinical ACTH conference, Philadelphia, Blakiston Company, 1950, pp. 529-535. Kass, E. H.; Ingbar, S. H.; and Finland, M.: Effects of Adrenocorticotropic Hormone in Pneumonia: Clinical, Bacteriological and Serological Studies, Ann. Int. Med. *33*:1081-1098 (Nov.) 1950.

2. (*a*) Spink, W. W.: ACTH and Adrenocorticosteroids as Therapeutic Adjuncts in Infectious Diseases, New England J. Med. *257*:979-983 (Nov. 14) 1957; ibid. *257*:1031-1035 (Nov. 21) 1957. (*b*) Kass, E. H., and Finland, M.: Corticosteroids and Infections, in Advances in Internal Medicine, Chicago, Year Book Publishers, Inc., 1959, vol. 9, pp. 45-73.

3. (*a*) Johnson, J. R., and Davey, W. N.: Cortisone, Corticotropin, and Antimicrobial Therapy in Tuberculosis in

Animals and Man: Review, Am. Rev. Tuberc. *70*:623-636 (Oct.) 1954. (*b*) Kass, E. H., and Finland, M.: Adrenocortical Hormones and Management of Infections, Ann. Rev. Med. *8*:1-18, 1957.

4. Evans, A. S.; Sprinz, H.; and Nelson, R. S.: Adrenal Hormone Therapy in Viral Hepatitis: Effect of ACTH in Acute Disease, Ann. Int. Med. *38*:1115-1133 (June) 1953.

5. Nelson, R. S.: Present Indications for Cortisone Therapy in Acute Viral Hepatitis, Ann. Int. Med. *46*:685-695 (April) 1957.

6. Coriell, L. L., and others: Use of Pituitary Adrenocorticotropic Hormone (ACTH) in Poliomyelitis, J. A. M. A. *142*:1279-1281 (April 22) 1950.

7. Hahn, E. O., and others: Effect of Cortisone on Acute Streptococcal Infections and Post-streptococcal Complications, J. Clin. Investigation *30*:274-281 (March) 1951.

8. Klemola, E., and Somer, P.: Treatment of Mumps Orchitis with Corticotropin and Cortisone, Nord. med. *56*:1128-1129 (Aug. 9) 1956.

9. Phillips, L. V.; Romansky, M. J.; and Nasou, J. P.: Staphylococcal Septicemia and Endocarditis Secondary to Cortisone-Treated Exfoliative Dermatitis due to Penicillin, in Antibiotics Annual 1954-1955, New York, Medical Encyclopedia, Inc., 1955, pp. 68-72. Kass and Finland.[3b]

10. Haggerty, R. J., and Eley, R. C.: Varicella and Cortisone, letters to the editor, Pediatrics *18*:160-162 (July) 1956.

11. Jawetz, E.: Effect of Cortisone on Therapeutic Efficacy of Antibiotics in Experimental Infections, A. M. A. Arch. Int. Med. *93*:850-862 (June) 1954.

12. Wagner, H. N., Jr., and others: Effect of Hydrocortisone upon Course of Pneumococcal Pneumonia Treated with Penicillin, Bull. Johns Hopkins Hosp. *98*:197-215 (March) 1956.

13. Kass, G. H.: Hypothermia Following Cortisone Administration, Am. J. Med. *18*:146-149 (Jan.) 1955.

14. Spink, W. W., and Hall, W. H.: Influence of Cortisone and Adrenocorticotropic Hormone on Brucellosis: II. Adrenocorticotrophic Hormone (ACTH) in Acute and Chronic Human Brucellosis, J. Clin. Invest. *31*:958-968 (Nov.) 1952.

15. Magill, G. B.; Kilough, J. H.; and Said, S. I.: Cortisone and Combined Antibiotic Therapy of Acute Brucellosis Melitensis, Am. J. Med. *16*:810-817 (June) 1954.

16. Johnson, J. R., and others: Corticotropin and Adrenal Steroids as Adjuncts to Treatment of Tuberculosis Meningitis, Ann. Int. Med. *46*:316-331 (Feb) 1957.

17. Lepper, M. H., and Spies, H. W.: Clinical Study of Use of Cortisone, Hydrocortisone, and Corticotropin in Treatment of Seriously Ill Patients with Infections, in Antibiotics Annual 1956-1957, New York, Medical Encyclopedia, Inc., 1957, pp. 447-454.

18. Rosenfeld, G.: In Vitro Influence of Bacterial Pyrogens on Adrenocortical Function of Perfused Calf Adrenals, Am. J. Physiol. *182*:57-62 (July) 1955.

19. Melby, J. C., and Spink, W. W.: Production and Catabolism of Cortisol in Experimental Endotoxin Shock, J. Clin. Invest. *37*:1791-1798 (Dec.) 1958.

20. Sokoloff, D.; King, B. D.; and Wechsler, R. L.: Symposium on Efficacy of New Drugs: Role of l-Norepinephrine in Treatment of Shock, M. Clin. North America *38*:499-514 (March) 1954.

21. Griffin, J. W., and Daeschner, C. W.: Meningococcal Infections, with Particular Reference to Fulminating Meningococcemia (Waterhouse-Friderichsen Syndrome) Treated with Cortisone and Norepinephrine, J. Pediat. *45*:264-272 (Sept.) 1954. Kanter, D. M.; Mauriello, D. A.; and Learner, N.: Acute Meningococcemia with Vascular Collapse: Analysis of 10 Recently Treated Cases, Am. J. M. Sc. *232*:674-687 (Dec.) 1956.

22. Levitin, H.; Kendrick, M. I.; and Kass, E. H.: Effect of Route of Administration on Protective Action of Corticosterone and Cortisol Against Endotoxin, Proc. Soc. Exper. Biol. & Med. *93*:306-309 (Nov.) 1956.

23. Dougherty, T. F., and Schneebeli, G. L.: Use of Steroids as Anti-inflammatory Agents, Ann. New York Acad. Sc. *61*:328-348 (May 27) 1955.

24. Bjorneboe, M.; Fischel, E. E.; and Stoerk, H. C.: Effect of Cortisone and Adrenocorticotrophic Hormone on Concentration of Circulating Antibody, J. Exper. Med. *93*:37-48 (Jan.) 1951. Fischel, E. E.; Stoerk, H. C.; and Bjoneboe, M.: Failure of Cortisone to Affect Rate of Disappearance of Antibody Protein, Proc. Soc. Exper. Biol. & Med. *77*:111-114 (May) 1951. Kass, E. H.; Kendrick, M. I.; and Finland, M.: Effects of Corticosterone, Hydrocortisone, and Corticotropin on Production of Antibodies in Rabbits, J. Exper. Med. *102*:767-774 (Dec.) 1955.

25. Benacerraf, B.; Halpern, B. N.; Biozzi, G.; and Benos, S. A.: Quantitative Study of Granulopectic Activity of Reticulo-endothelial System: Effect of Cortisone and Nitrogen Mustard on Regenerative Capacity of R.E.S. After Saturation with Carbon, Brit. J. Exper. Path. *35*:91-106 (April) 1954.

J.A.M.A. *170*:1179 (July 4) 1959.

CHEMICAL LABORATORY

Monographs and Tests

The Chemical Laboratory has authorized publication of the following statement.

WALTER WOLMAN, PHD., *Director.*

Monographs of tests and assays for new and nonofficial drugs adopted by the Chemical Laboratory of the American Medical Association represent an expression of opinion as to what might constitute adequate tests and assays to serve as a reference guide to those interested in the identity and quality of a new and nonofficial drug.

Complete monographs are published in the journal *Drug Standards* for those interested in the details of the procedures. Monographs on the following drugs have appeared in the March-April, 1959, issue of that journal, except for the monograph on chloroprocaine hydrochloride which appeared in the January-February, 1959, issue. The cooperation of the listed pharmaceutical firms that furnished samples and data is acknowledged.

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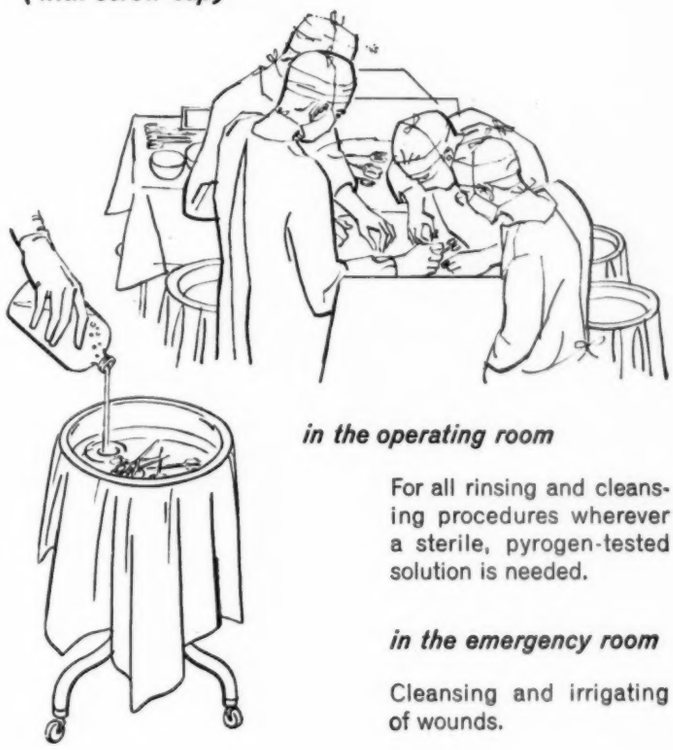

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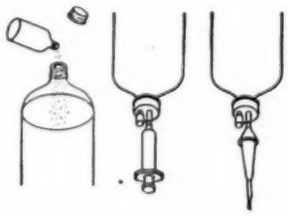

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PHARMACIST—Male, single. Hospital pharmacy experience. B.S. Registered in Mo. and Ill. Will locate anywhere. PW-196

CHIEF PHARMACIST—Male, married. B.S. received in 1953. Four years' hospital pharmacy experience. Prefers Eastern part of country. Registered in Pa. and N.Y. PW-195

STAFF PHARMACIST—Female, single. B.S. Hospital pharmacy experience. Prefers central southern part of Canada. Registered in Philippines. PW-194

CHIEF PHARMACIST—Male, married. B.S. Ten years' hospital pharmacy experience. Registered in Pa., N.Y. and Fla. Prefers to locate in Pa. and N.Y. PW-193

CHIEF PHARMACIST—Male, single. A.B. degree received in 1949. Six years' hospital pharmacy experience. Prefers teaching hospital. Registered in Mass. and Conn. Desires to locate in East. PW-192

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. B.S. received from City College of N.Y. Hospital pharmacy experience. Registered in N.Y. Prefers to locate in Northeast. PW-191

STAFF PHARMACIST—Male, married. B.S. One years' hospital pharmacy experience. Registered in N.Y. and Fla. Prefers to locate in Fla. PW-190

CHIEF PHARMACIST—Male, single. B.S. Registered in Minn. and N. D. Prefers foreign job anywhere. PW-189

CHIEF PHARMACIST—Male, married. B.S. Six years' hospital pharmacy experience. Prefers to locate in Calif. Registered in Calif. and Ill. PW-187

PHARMACIST—Male, single. B.S. received in 1956. One years' hospital pharmacy experience. Would prefer Chicago area. Registered in Mich. PW-186

CHIEF PHARMACIST—Male, married. M.S. Hospital experience. Prefers to locate in East. Registered in N.Y., Mich., N.J., and Fla. PW-184

PHARMACIST—Male, married. B.S. Three years' experience in Sudan Interior Mission Hospital. Prefers to locate in South particularly S.C. Registered in S.C. PW-183

STAFF OR ASST. CHIEF PHARMACIST—Female, single. B.S. Three years' hospital experience. Prefers to locate in Midwest. Registered in Mo. PW-181

PHARMACIST—Male, married. B.S. Interested in career in hospital pharmacy. Prefers to locate in East. Registered in N.Y. and Ill. PW-180

CHIEF PHARMACIST—Male, single. B.S. Four years' hospital experience. Interested in manufacturing and administration. Registered Conn. Prefers Northeast section of country. PW-179

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ASST. CHIEF OR STAFF PHARMACIST—Female, single. B.S. Registered in La. and Ohio. Prefers Ohio and Northern part of country. PW-176

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PHARMACIST—Butler University graduate with Ph.C. degree. Registered in Ill., Ky., Ind., Ore. Prefers to locate in Midwest. PW-173

PHARMACIST—Graduate Philadelphia College of Pharmacy and Science 1959; 22 months' hospital pharmacy experience. Registered in Pa. Desires position in the East. PW-172

STAFF PHARMACIST—Female. 1957 graduate of the University of Buffalo College of Pharmacy. Registered in N. Y. Prefers to locate in the East. PW-171

PHARMACIST—Registered in Iowa and S.D. Prefers to locate in Mich., Colo. or Ariz. Management experience. PW-167

PHARMACIST—Female. Graduate of the University of Idaho, 1954. Registered in Ill. Hospital experience. Prefers Chicago area. PW-166

PHARMACIST—Graduate of Long Island University and the University of Louisville. Prefers position in Ky. or Va. PW-165

CHIEF OR ASST. CHIEF PHARMACIST—Female. B.S. and M.S. Purdue University. Ten years' hospital pharmacy experience. Registered in Ind. and Ky. PW-164

STAFF PHARMACIST—Young female pharmacist from Taiwan would appreciate position in U.S. teaching hospital with opportunity to learn more about hospital pharmacy. Has experience as manufacturing pharmacist at National Taiwan University Hospital. PW-163

STAFF OR ASST. CHIEF PHARMACIST—Male. Served hospital pharmacy internship. One year's additional experience. Registered in Minn. and Wash. Prefers to locate in West. PW-162

PHARMACIST—Male. Registered in La. and Mo. Experienced. Prefers Midwest. PW-161

STAFF PHARMACIST—Male, married. Registered N. Y. and N. J. Prefers New England. PW-157

CHIEF PHARMACIST—Female, single. B.S. Registered R. I. Eight years' hospital pharmacy experience. PW-156

ASST. CHIEF PHARMACIST—Male, single. Registered N. Y. and Vt. Served hospital pharmacy internship, now employed part-time staff pharmacist. Prefers Eastern part of country. Has M.S., 4 years' hospital pharmacy experience. PW-154

ASST. PHARMACIST—Male, married. B.S. Served hospital pharmacy internship. Experienced hospital pharmacist, research pharmacist and retail pharmacist. PW-151

CHIEF PHARMACIST—Male, married. B.S. Ten years' hospital pharmacy experience. Registered Mass., Ill., Mo., Ky., Tenn. and Va. PW-150

PHARMACIST—Male, single. B.S. pharmacy, June 1959. Locate East. PW-149

ASST. CHIEF OR CHIEF PHARMACIST—Single, male. Registered in D. C., Ill., Md., and Pa. Graduate University of Pittsburgh in 1953; experience in research. Prefers North and East. PW-148

CHIEF PHARMACIST—Registered in Mo. and Ill. Ph.G. degree. Eight years' experience in hospital pharmacy. PW-147

STAFF PHARMACIST—Male, single. Completed military requirements. Hospital pharmacy experience. Prefers East. PW-146

CHIEF PHARMACIST—Registered in N. J. Any location. Six years' experience in hospital pharmacy. PW-145

CHIEF PHARMACIST—Prefers N. Y. or N. J. area. Over 20 years' experience as chief pharmacist and purchasing agent. Graduate St. John's University College of Pharmacy. Registered in N. Y. and N. J. PW-144

ASST. CHIEF PHARMACIST—Male, married. B.S. pharmacy. Registered N. Y. Hospital and retail experience. Locate N. Y. State. PW-142

CHIEF PHARMACIST—Male, married. B.S. Conn. registration. Five years' hospital pharmacy experience. Prefers Northeast section of country. PW-140

PHARMACIST—Male, single. Registered Conn. and N. J. Five years' hospital pharmacy experience. B.S. Prefers Conn. or Texas. PW-123

ASST. DIRECTOR OR DIRECTOR OF PHARMACY SERVICES—Male, single. B.S. Retail and five years' hospital experience. Registered Ill. PW-119

CHIEF PHARMACIST—Female, single. Registered in Pa. and Ohio. Twelve years' experience as Chief Pharmacist. Desires to locate in Pa. or Ohio. PW-111

STAFF PHARMACIST—Female, single. Registered Mo. B.S. Hospital pharmacy experience. Desires to locate in Midwest. PW-104

positions open

STAFF PHARMACIST—269 bed nonprofit general hospital located in Calif. Duties include filling ward orders, individual prescriptions, outpatient prescriptions and narcotic orders. Applicant must have B.S. in pharmacy, 1 year's experience or preferable hospital pharmacy internship. Willingness to work week ends and nights as required. Male or female. Forty to forty-eight hour week, two weeks' vacation after one year, 6 paid holidays, 12 days sick leave, hospital health insurance plan. PO-157

CHIEF PHARMACIST—190 bed general hospital located in Wis. Pharmacist will have complete control of the pharmacy, responsible for dispensing, charges, inventory and purchasing. Work with Medical Staff to formulate policies for dept. with administrative approval. Capable of cooperating with the Medical Staff, helping the Medical Staff keep abreast of advances in the field, and guiding and directing the Nursing Staff in their usage. Thirty-six to forty-four hours per week, two weeks' vacation after one year, Municipal Pension Plan, insurance, 10 days sick leave per year accumulative to 30. Must be registered in Wis. PO-156

CHIEF PHARMACIST—164 bed nonprofit corp. general short-term hospital located in Ohio. This is a small pharmacy operated by one pharmacist and an assistant. Responsible for complete operation of pharmacy including purchasing, dispensing, pricing, and control of all pharmaceuticals used in hospital. Must be registered. Forty hour week, vacation, paid life and sickness and accident insurance after 2 years' employment. PO-155

SUPERVISOR OUTPATIENT PHARMACY OR STAFF PHARMACIST—236 open bed general state hospital located in Arkansas. Supervisor's duties include some teaching of pharmacy students, supervise one other pharmacy and administer this subdivision which fills about 200 prescriptions daily. Must be an especially intelligent and well trained pharmacist preferably with an internship in hospital pharmacy. Staff pharmacist rotates among the various subdivisions of the hospital pharmacy: outpatient pharmacy, inpatient pharmacy, non sterile manufacturing and sterile manufacturing. Should be a good pharmacist, intelligent, interested in hospital pharmacy professionally. Forty hour week, vacation, 6 paid holidays per year, opportunity to learn in one of the most active hospital pharmacy depts. in the country, after 2 years participate in retirement program which provides essentially a 6% increase in salary, close relationships with schools of pharmacy, medicine and nursing. PO-154

ASST. CHIEF PHARMACIST—340 bed general hospital located in Syracuse. Assist chief pharmacist in dispensing drugs and pharmaceutical supplies, no manufacturing. Must be registered in N. Y. Forty-four hour week, 2 weeks' vacation, sick leave, holidays, retirement plan, good promotional possibility, stable job and excellent working conditions. PO-153

STAFF PHARMACIST—215 bed general hospital. Compound and dispense drugs, manufacture pharmaceuticals and assist in all other pharmaceutical duties in the pharmacy. B.S. required. Must be eligible for licensure in Pa. Forty hour week, three weeks' vacation, 7 holidays, 10 days paid sick leave, annual physical examinations, merit salary increases. PO-152

ASST. CHIEF PHARMACIST—220 bed general hospital located in Honolulu, Hawaii. Compounds and dispenses medicines and preparations. Responsible for administration of dept. in absence of chief pharmacist. Forty hour week, 3 weeks' vacation, paid sick leave, medical insurance, retirement. Must be eligible for licensure in Hawaii. PO-151

ASST. PHARMACIST—250 bed general hospital. Forty hour week, 2 weeks' vacation, sick leave and 6 paid holidays per year. Must be registered in N. C. PO-150

ASST. CHIEF PHARMACIST—156 bed (expanding to 200) general hospital located in Ill. Forty hour week, 2-4 weeks' vacation, Blue Cross Insurance, cafeteria privileges, and sick leave. Must be licensed. PO-149

STAFF PHARMACIST—370 bed general private hospital. Moving to new 400 bed hospital in Jan. 1960. Compound and dispense medicines and preparations according to prescriptions ordered by medical staff either in central pharmacy or in pharmacy unit on a 100 bed floor. Related work such as keeping supply levels up, manufacturing solutions, etc. Outstanding opportunity for career in ethical pharmacy. Forty hour week, two weeks' vacation after one year, three weeks' after five years, 7 paid holidays, sick leave, employee credit union, merit increases. Must be eligible for licensure in Calif. PO-148

ASST. CHIEF PHARMACIST—440 bed teaching hospital. Must be registered in Mo. Forty-four hour week, three weeks' vacation, one week sick leave, state retirement and insurance. PO-147

ASST. CHIEF PHARMACIST—250 bed general hospital located in N. Y. Male preferred. Registration in N. Y. required. Ability to pass N. Y. State Civil Service examination. Duties include filling ward orders, patient prescriptions, checking stock and small volume parenteral solution manufacturing. Forty hour week, 3 weeks' vacation, annual sick leave, 7 paid holidays, retirement plan, group insurance available. Located outside city. Some housing available on premises. PO-146

STAFF PHARMACIST—650 bed general hospital located in Chicago, Ill. B.S. required. Must be eligible for registration in Ill. Male under 35 years preferred. Duties include general dispensing (inpatient and outpatient) and teaching. Forty hour week, one month vacation with pay, free medical benefits, retirement program. PO-145

CHIEF PHARMACIST—110 bed general hospital located in Ill. Must be eligible for licensure in Ill. Duties include administration of the dept., purchasing, maintaining inventory records, preparing scientific and educational exhibits, liaison between medical staff and administration, assisting in establishment and maintenance of a formulary and a formulary committee. Forty to forty-four hour week, two weeks' vacation. PO-144

CHIEF PHARMACIST—145 bed general hospital. Male preferred. Will have complete responsibility of pharmacy dept. Must have registration in Ohio. Forty-four hour week, vacation, sick leave and paid holidays. PO-143

ASST. CHIEF PHARMACIST—166 bed hospital located in Montana. Forty hour week, two weeks' vacation. PO-142

CHIEF PHARMACIST—155 bed hospital located in N.J. Must be registered in N. J. Dispense drugs to nursing units, maintain a formulary and confer with Medical Staff Formulary Committee, maintain up-to-date adequate inventory records, administer alcohol and narcotic storage and issuance, interview drug representatives and make purchases of drugs subject to administrator's approval, establish together with the administrator appropriate charges for drugs, and issue inpatient and outpatient drug charge slips. Generous benefits. PO-141

ASST. CHIEF PHARMACIST—262 general hospital located in Ind. Duties include general Rx work, limited manufacturing, assisting in teaching student nurse program, assisting in narcotic security. Forty to forty-eight hours per week, three weeks' vacation after three years. Generous benefits include sick leave, paid holidays, hospitalization and retirement. PO-140

ASST. CHIEF PHARMACIST—Woman preferred. Must have Pa. registration. Duties include filling prescriptions and small volume of manufacturing. Forty hour week, 7 holidays per year, 7 sick days with pay per year. PO-139

CHIEF PHARMACIST—65 bed (increasing to 100 bed) general hospital located in N. Y. Carry out functions of pharmacy dept. Opportunity to be named Chief Purchasing Agent and be chief purchaser for the hospital. Forty-hour week, up to 3 weeks' vacation. Located in low cost living area. PO-138

CHIEF PHARMACIST—495 bed general hospital located in Va. Responsible to superintendent for management of pharmacy personnel, solution manufacturing, purchase of all pharmaceutical items and supervision of compounding and dispensing drugs. Lecture student nurses. Must be registered. Varied working hours, 3 weeks' vacation. Benefits include meals while on duty, hospitalization insurance, if single—room available. PO-137

STAFF PHARMACIST—250 bed general hospital located in Rochester, N. Y. Must be registered in N. Y. Forty hour week. Liberal personnel policies. PO-136

CHIEF PHARMACIST—70 bed general hospital, located in N. C. Responsible for establishing a pharmacy dept. and assisting in the purchasing dept. Generous benefits. PO-135

CHIEF PHARMACIST—150 bed general hospital located in N. M. To assume complete charge of purchasing and distributing drugs. PO-134

STAFF PHARMACIST—75 bed general, private hospital located in Ind. State registration required. Male or female. PO-131

CHIEF PHARMACIST—120 bed general, non-profit hospital. Individual will have complete charge of ordering, dispensing and charging of medical supplies. Male or female. Registration in Ohio required. Forty to forty-eight hour week, two weeks' vacation, other generous hospital benefits. PO-129

ASST. CHIEF PHARMACIST—325 bed hospital. Forty hour week, 4 weeks' vacation. Must be eligible for registration in Pa. PO-128

CHIEF PHARMACIST—185 bed private non-profit hospital located in Va. Prefer applicant with hospital pharmacy internship and one year's experience. PO-126

STAFF PHARMACIST—450 bed general hospital located in Ohio. PO-124

ASST. CHIEF PHARMACIST—3,300 bed psychiatric hospital. To assist in the reorganization of the dept. Eligible for registration in Ohio. Two years' experience preferred. PO-123

CHIEF PHARMACIST—60 bed mission hospital operated by Presbyterian National Missions; extensive outpatient department; on Navajo Indian Reservation near Gallup, N. M. Qualified to register in Ariz.; single man or woman, challenged by service rather than benefits. PO-122

STAFF PHARMACIST—150 bed general hospital. Only female considered. Must be eligible for Ill. registration. Forty hour week, 2 weeks' vacation. PO-116

ASST. CHIEF PHARMACIST—425 bed general hospital. Duties include dispensing and supervision of special projects. Prefer male applicant with internship in hospital pharmacy. Unique opportunity to obtain experience. PO-115

CHIEF PHARMACIST—150 bed general hospital. To assume complete responsibility for the pharmacy department. Three weeks' vacation, discount on meals and hospitalization. PO-114

CHIEF PHARMACIST—340 bed general hospital in South, affiliated with medical school. Outpatient clinic and hospital pharmacy internship program. PO-112

STAFF PHARMACISTS—TWO—Eligible for licensure in West Va. and Ky. PO-111

STAFF PHARMACIST—215 bed general hospital expanding to 35 more beds. N. Y. registration required as well as hospital experience. Forty hour week, 2 weeks' vacation. PO-104

ASST. CHIEF PHARMACIST—152 bed general hospital expanding to 180 beds. Registration in Neb. required. Forty hour week, 2 weeks' vacation. PO-101

STAFF PHARMACIST—400 bed general hospital located in Iowa. Forty hour week, 2 weeks' vacation. PO-99

CHIEF PHARMACIST—425 bed hospital. Male preferred. Mo. registration required. Will train good applicant. Forty-hour week. PO-98

STAFF PHARMACIST—400 bed general hospital. Eligible registration in Fla. Forty hour week. PO-96

STAFF PHARMACIST—500 bed general hospital located in Okla. B.S. required. Forty hour week. PO-95

ASST. CHIEF PHARMACIST—315 bed general hospital. Registration in Iowa required. Experience desirable. Forty hour week, 2 weeks' vacation. PO-92

STAFF PHARMACIST—400 bed general hospital. Internship in hospital pharmacy preferred. Eligible for Tex. registration. Forty hour week; 2 weeks' vacation. PO-90

ASST. CHIEF PHARMACIST—237 bed general hospital in West Va. Female desired. Forty-four hour week, 2 weeks' vacation. PO-77

STAFF PHARMACIST—335 bed hospital located in Fla. Duties include responsibilities in outpatient department and parenteral solution room. Forty hour week, 2 weeks' vacation and 1 meal daily. PO-75

STAFF PHARMACIST—325 bed research hospital. Minimum 2 years' experience, preferably in hospital pharmacy. N. Y. registration required. Duties include manufacturing sterile solutions and assisting in product development. Research work beyond forty hour week available at hourly rate. PO-61

CHIEF PHARMACIST—88 bed hospital located in Pa. Planning expansion to 125 beds for general patients and 40 beds for chronic patients. Possibility for pharmacist to serve as Asst. Adm. in charge of Purchasing, Central Supply, and Store Room. Forty hour week, 2-4 weeks' vacation. Young man preferred. PO-59

ASST. CHIEF PHARMACIST—Large voluntary hospital located in Brooklyn. Must be eligible for registration in N. Y. Supervisory ability needed. Thirty-five hour week, 2 weeks' vacation; 10 days' sick leave; 9 holidays. PO-51

STAFF PHARMACIST—460 bed general hospital in Mass. Forty hour week, 2 weeks' vacation, other benefits. PO-40

ASST. CHIEF PHARMACIST—310 bed general hospital located in Va. Forty hour week, 2 weeks' vacation, 3 weeks' sick leave, 6 holidays. Also STAFF PHARMACIST in same hospital. Forty hour week, 2 weeks' vacation. PO-35

STAFF PHARMACIST—550 bed general hospital located in Ohio. Forty hour week; 2 weeks' vacation. PO-34

CHIEF PHARMACIST—350 bed hospital. Must be eligible for licensure in N. J. Interest in manufacturing. Forty-four hour week, 2 week's vacation. PO-6

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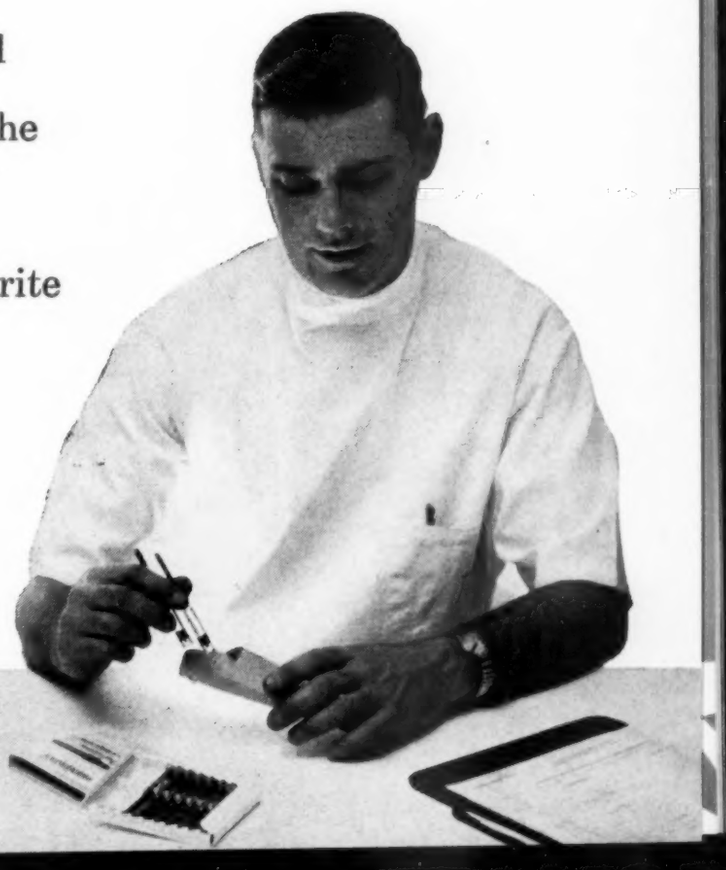

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